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Pathways to Psychosis

Examining the Effect of Childhood Trauma and Abnormal Belief-Updating Processes on Psychosis

Pathways to Psychosis: Examining the Effect of Childhood Trauma and Abnormal Belief-Updating Processes on Psychosis

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Abstract

There is a body of evidence showing that childhood trauma is associated with psychotic experiences (PEs). Establishing whether this association is causal and what mechanisms mediate this relationship is needed to understand how psychosis develops and help inform interventions to mitigate the risk of PEs.

The first study in this thesis investigates whether exposure to interpersonal violence and neglect is causally associated with PEs, whether there are sensitive periods of exposure, and if different types of trauma are differentially associated with PEs. The subsequent studies in this thesis examine whether information-processing biases are associated both with trauma and PEs, and whether these biases lie on the causal pathway from trauma to PEs.

Analyses were carried out using data from ALSPAC, a large UK birth cohort. A systematic review and meta-analysis of childhood trauma and psychosis-related information-processing biases was also conducted.

Childhood trauma was associated with PEs and this was largely unchanged after adjustment for confounders. The greatest increase in PE risk was associated with exposure to multiple types of trauma, consistent with a dose-response relationship. There was little evidence to support the presence of sensitive periods of risk or of differential effects of specific types of trauma. When examining information-processing biases I found that an increased expectation of change (reversal) and sub-optimal belief-updating (decision noise) were associated with PEs, and not explained by confounding. Childhood trauma was also associated with greater decision noise, but not with the other belief-updating processes examined. However, there was little evidence that decision noise mediated the relationship between trauma and PEs. The systematic review provided some evidence that childhood trauma is associated with a bias to attribute the cause of events to external factors, but not with the other biases examined.

I conclude the thesis with a critical evaluation of the results, within the context of the studies' strengths and limitations, and discuss the extent to which they support a causal relationship between exposure to trauma and PEs, and whether abnormal-belief updating processes are on this hypothesised pathway.

Further research should utilise interdisciplinary approaches and longitudinal data to establish what mechanisms contribute to the psychosis pathway in order to identify targets for intervention that can mitigate the effect of trauma exposure on PE and other mental health outcomes.

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Author’s Declaration

I declare that the work in this thesis was carried out in accordance with the requirements of the University's Regulations and Code of Practice for Research Degree Programmes and that it has not been submitted for any other academic award. Except where indicated by specific reference in the text, the work is the candidate's own work. Work done in collaboration with, or with the assistance of, others, is indicated as such. Any views expressed in the dissertation are those of the author.

Signed …………………………….. Date………………………………

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Publications associated with the thesis

<u>The following article is published:</u>

Study I: ‘Association of Trauma Type, Age of Exposure, and Frequency in Childhood and Adolescence With Psychotic Experiences in Early Adulthood’

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<u>The following articles are prepared and awaiting submission:</u>

Study II: ‘Childhood Trauma and Cognitive Biases associated with Psychosis: A Systematic Review’

Jazz Croft, David Martin, Paul Madley-Dowd, Daniela Strelchuk, Jonathan Davies, Jon Heron, Christoph Teufel, Stanley Zammit

Study III: ‘The association between exposure to trauma, abnormal belief-updating, and psychotic experiences: findings from computational analyses of a large UK birth cohort’

Jazz Croft, Jon Heron, Christoph Teufel, Rick Adams, Paul Fletcher, Stanley Zammit

Other publications completed during the thesis as co-author

'Systematic review and meta-analysis of the relationship between genetic risk for schizophrenia and facial emotion recognition'
David Martin, **Jazz Croft**, Alice Pitt, Daniela Strelchuk, Sarah Sullivan, Stan Zammit
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'Childhood Trauma and Trajectories of Depressive Symptoms Across Adolescence'
Alex Kwong, Jennifer Maddalena, **Jazz Croft,** Jon Heron, George Leckie, *medRxiv,* 2019 doi: https://doi.org/10.1101/19002519

'Genetic liability to schizophrenia is associated with exposure to traumatic events in childhood'
Hannah M Sallis, **Jazz Croft,** Alexandra Havdahl, Hannah Jones, Erin Dunn, Stanley Zammit, Marcus Munafò, *medRxiv*, 2019 doi: https://doi.org/10.1101/19006577

Contribution to research

The broad aims of the thesis were conceived as part of the MRC grant 'pathways to psychosis' (PI: Stanley Zammit), I developed these themes to address gaps in current literature and used data collected as part of the grant for study III. My contribution to this research: I conceived each chapter either jointly or in whole and led all the chapters in this thesis. I had sole access to the data used; cleaned, coded and prepared the data where necessary; conducted all the statistical analyses; developed search protocols; screened all studies and extracted data; interpreted the data either jointly or in whole; and had executive decision on all edits and changes to the final drafts of each chapter/manuscript.

Chapter 1 Introduction

1.1 Psychosis

Psychotic disorders, including schizophrenia, bipolar disorder, and depression with psychotic symptoms, are severe and often extremely distressing psychiatric illnesses. The estimated lifetime prevalence for all psychotic disorders is approximately 3% (Perälä et al., 2007; van Os et al., 2009). The lifetime prevalence of schizophrenia, perhaps the most severe psychotic disorder, has been estimated to range between 0.5%–1.6% (Hjorthøj et al., 2017) and has a point-prevalence of 1.4-4.6 per 1000 individuals (Jablensky, 2000). The estimated number of prevalent cases globally, based on estimates from 188 countries, in 2013 was 23.6 million (Global Burden of Disease Study 2013 Collaborators, 2015).

The onset of schizophrenia peaks around early adulthood and is lower for men (between 21-25 years of age) compared to women who peak at both ages 25 to 30 years and after 45 years of age (Kirkbride et al., 2012; Li et al., 2016). The early life onset and often recurrent disease course leads to a relatively high prevalence in relation to incidence; the median incidence of schizophrenia is estimated to be 15.2 per 100,000 people, although there is a large variation in incidence rates worldwide (Mcgrath et al., 2008).

While psychotic disorders are relatively rare, their global health burden is high due to the distress experienced by the individual, the burden of care on caregivers (Lauber et al., 2005), the economic cost and the extent to which the illnesses and treatments such as anti-psychotic medications contribute to a reduced quality of life (Millier et al., 2014). Schizophrenia, for example, is a leading cause of disability estimated to be associated with an average of 14.5 years of potential life lost (95% CI: 11.2%-17.8%; Hjorthøj et al., 2017; Chong et al., 2016) and an increased risk of death by suicide or accident (Brown, 1997; Caldwell & Gottesman, 1990).

Psychotic disorders are characterised by the presence of psychotic symptoms, most notably hallucinations and delusions. Hallucinations are abnormal perceptions that are generated by an individual in the absence of external stimuli and which feel as real as regular perceptual experiences. Hallucinations can occur in any sensory modality (visual, auditory, olfactory, gustatory and tactile) and can vary in their duration, content and the extent to which they are distinguishable from normal (non-psychotic) experiences.

Delusional beliefs are beliefs firmly held by an individual that are false and irrational that are not accounted for by cultural or religious background, and are resistant to contrary information (Gelder, 1996). Delusions are classified according to the content of the belief, for example, beliefs that others are trying to cause harm (persecutory delusions), or beliefs of extreme self-importance (grandiose delusions). As with hallucinations, delusional beliefs can vary in the conviction in which they are held and the extent to which they differ from normal (non-psychotic) experiences.

Psychotic experiences, such as hallucinations and delusions, can occur even when individuals do not meet clinical thresholds for a psychotic disorder. For example, hallucinations are also observed in the context of using certain drugs, can occur in medical disorders such as Parkinson’s disease and dementia, and are known to be a common response when mourning the death of a loved one (Castelnovo et al., 2015; Teeple et al., 2009). Population-based studies show that while psychotic disorders are relatively rare, psychotic experiences are not uncommon in the general population (see below).

1.2 Psychotic Experiences

Studies of psychotic phenomena in the general population often use terms interchangeably and inconsistently, which makes interpreting previous literature challenging. In this thesis, I will refer to the following terms and associated definitions:

i) *Psychotic experiences* (PEs) refers to the presence of hallucinations or delusions, as assessed using a semi-structured interview. These experiences might not necessarily be distressing and include experiences that might not lead to help-seeking, require a clinical need for care, or meet criteria for a clinical disorder.

ii) *Psychotic symptoms* are symptoms described above that cause impairment in functioning and might require a need for care, but not necessarily indicate the presence of a psychotic disorder.

iii) *Psychotic-like experiences* (PLEs) are experiences assessed by fully structured assessment (interview or questionnaire) which do not provide the opportunity for cross-questioning to elicit if experiences are truly psychotic.

1.2.1 The epidemiology of psychotic experiences and psychotic-like experiences

The estimated prevalence and incidence of PEs/PLEs varies widely across studies and is substantially higher than for psychotic disorder. Meta-analyses estimate that the lifetime risk of PEs in the general population is between approximately 5%-10% and the median one-year incidence is between 0.025-0.03 (Linscott & Os, 2013; Maijer et al., 2018; van Os et al., 2009). However, there is substantial variation in prevalence estimates, as shown in Van Os and colleagues' (2009) meta-analysis that reported a median estimated prevalence of 8.4% and an interquartile range (IQR) of 3.5% - 20.9%. A later meta-analysis reported that the prevalence of PLEs/PEs varied according to the method of data collection; the median prevalence for PLEs/PEs collected by interview was 3.8%, and self-reported PLEs was 11.9% (Linscott & Os, 2013).

The prevalence of PLEs/PEs in childhood is estimated to be higher than in adult populations, with a median prevalence of 17% in ages 9-12 years and 7.5% during adolescence (age 13-18 years; Kelleher et al., 2012). In studies of the ALSPAC cohort, the estimated prevalence of PEs rated by interviewers as suspected or definite at age 12 years was 13.7% (Horwood et al., 2008) and was 9.2% at age 18 years (Zammit et al., 2013). The estimated prevalence of PEs rated as definitely present in the ALSPAC cohort was lower at both age points: 5.6% at age 12 years and 4.7% at age 18 years (Horwood et al., 2008; Zammit et al., 2013).

It has been observed that approximately 20% of PEs/PLEs are persistent (Linscott & Os, 2013). Of the participants in the WHO World Mental Health survey who reported PEs, 32.2% reported only one occurrence of PEs in their lifetime and 31.8% only 2–5 occurrences (McGrath et al., 2015).

1.2.1.1 Variation in measures of sub-clinical psychotic symptoms

The wide range of methods used to assess PEs and PLEs is likely to contribute to the wide inter-quartile range of estimates in the meta-analyses of estimated prevalence and incidence. In Linscott and colleagues' (2013) meta-analysis, the method of data collection accounted for 19.7% of the variance in the pooled analysis and found association between both smaller sample size and the use of convenience sampling with an increased likelihood of reporting PLEs assessed by questionnaire; this relationship was not observed for studies that used interview methods.

A systematic review that examined self-report measures of PLEs (Lee et al., 2016) reported that, of 76 studies, 41 different assessment tools were used. Based on the study authors' assessment, a large proportion of the studies (n=51, 67%) used quantitative measures of PLEs that did not define PLEs by a pre-determined quantitative threshold. Of the 22 studies that did have a pre-determined criteria to define the presence of PLEs, 13 studies adopted cut-off scores to define PLEs, 6 identified PLEs according to performance of participants (i.e. highest decile of PLE assessment score), and three studies used the endorsement of specific items on the assessment tools to define PLEs. The review illustrates that there is a lack of a 'gold standard' measure of PLEs in the general population and that the criteria for what a PLE is varies between studies and is often not defined by study authors. Heterogeneity in the measurement of PLEs limits how generalisable estimates of PLEs in the general population are and raises issues about methodology and replicability of studies of PLEs.

1.2.2 The psychosis continuum

The observation that psychotic and psychotic-like phenomena are not uncommonly reported in the general population has been interpreted as evidence of a continuum model of psychosis. The psychosis continuum model characterises psychosis as a symptom dimension that varies in severity and persistence and is distributed on a continuum across the population (Kaymaz & van Os, 2010; van Os et al., 2009). Infrequent PLEs are at the less severe end of the continuum, while more persistent, distressing and impairing experiences that meet criteria for a psychotic disorder and require medical treatment are at the more severe end.

The pattern of distribution of the psychosis continuum is a subject of discussion (DeRosse & Karlsgodt, 2015; Lawrie, 2016). It is likely that the distribution of the psychosis continuum is skewed at the most severe end, and exists as an extended phenotype, as opposed to a normal distribution in the general population. If the distribution of psychotic phenomena was normally distributed, a much greater proportion of the population would be expected to report PEs or PLEs than is observed.

As will be detailed in subsequent sections, there is evidence to suggest that similar risk factors contribute to the aetiology of psychotic symptoms across the psychosis continuum in clinical and sub-clinical contexts. These risk factors include cannabis use, exposure to childhood trauma, perinatal complication (maternal infection and diabetes) and exposure to urban environments (Dorrington et al., 2014; Jones et al., 2018; Newbury et al., 2019; Varese et al., 2012). These findings suggest that there may be overlapping mechanisms on the psychosis pathway for both clinical and sub-clinical psychotic outcomes. There is weaker evidence to suggest that there is an association between an increased genetic risk for schizophrenia and less severe sub-clinical psychotic symptoms; a recent study found that genetic risk for schizophrenia was only associated with PEs that are frequent or distressing (Legge et al., 2019).

1.2.2.1 Do PEs predict psychotic disorder?

Linscott and colleagues' (2013) meta-analysis estimates that 7.4% of individuals who report PLEs or PEs at baseline go on to develop a psychotic disorder. Based on analyses of the ALSPAC cohort, the predictive values of PEs at age 12 years for psychotic disorder at age 18 years were too low (approximately 5.5% - 22.8%) to have the clinical utility to be the basis of targeted interventions to prevent psychotic disorder (Zammit et al., 2013). For those who report PEs, the risk of developing a psychotic disorder is estimated to be increased by around four times (Healy et al., 2019; Kaymaz et al., 2012). In a longitudinal study conducted over eight years, a third of those with clinical symptoms of psychosis had reported PLEs at a previous timepoint, indicating that PLEs frequently precede the development of psychotic disorder (Dominguez et al., 2011). This evidence has been interpreted as supportive of a continuum view of psychosis.

1.2.2.2 Why is it important to investigate the aetiology and epidemiology of psychotic experiences?

Studies of sub-clinical symptoms of psychosis can help to inform understanding of psychosis and address limitations of studies in clinical populations. As psychotic disorder is a rare outcome, cohort studies that can adequately address questions relating to aetiology and symptom development require prohibitively large sample sizes and long durations of follow-up, especially for early-life exposures.

As PEs are more common than psychotic disorder, it is possible to study them repeatedly over time in a longitudinal study design, as has been undertaken for example in the ALSPAC cohort (detailed in Chapter 5) and the NEMESIS cohort based in the Netherlands (Wigman et al., 2012; Zammit et al., 2013), to study their persistence and development from incidence of PE through to onset of psychotic disorder. While findings from studies of PEs should not be interpreted as directly translatable to studies of clinical populations, they can help test hypotheses that may have implications across the psychosis continuum.

The importance of understanding PEs is not confined to their association with an increased risk of psychotic disorder. There is evidence that PEs are associated with other negative outcomes, including poorer educational attainment, behavioural difficulties, the development of non-psychotic mental health disorders, increased medical help-seeking and suicidal ideation (Bromet et al., 2017; Davies et al., 2018; Healy et al., 2019; Kirli et al., 2019; Unterrassner et al., 2017). In a meta-analysis of 14 studies of PEs and subsequent mental health outcomes, PEs were associated with an approximately three-fold increase in the risk of developing a non-psychotic mental health disorder (Healy et al., 2019). The association between PEs and a wide range of mental health outcomes illustrates the importance of understanding causal risk factors for PEs as this may have transdiagnostic implications for interventions that may mitigate the risk of a variety of mental health disorders.

1.3 Psychosis aetiology

Most research relating to the aetiology of psychotic disorders to date has examined schizophrenia. The focus of this section will, therefore, reflect this, although I will highlight wherever important differences exist in the evidence of aetiology for different psychotic disorders. I will also compare findings of the aetiology of psychotic disorders with that for PEs in the general population.

1.3.1 Schizophrenia

Schizophrenia is a long-term mental health disorder characterised by the presence of thought disorder, delusions and hallucinatory voices. Other indicators of schizophrenia include incoherent speech, persistent hallucinations and negative symptoms (apathy, affective blunting and paucity of speech; World Health Organization, 1992).

Rates of schizophrenia have been observed to be higher in different populations. Men have higher rates of schizophrenia than women (ratio 1.4:1; Aleman, 2014; McGrath et al., 2008) and rates of schizophrenia are elevated in individuals who have migrated or are of an ethnic minority status (Bourque, Ven, & Malla, 2011; Dykxhoorn et al., 2018; Kirkbride et al., 2012; McGrath et al., 2008).

Based on pooled estimates, risk of schizophrenia is approximately two times higher in urban areas compared to rural areas and this risk increases according to the duration of exposure to urban environments (March et al., 2008; Vassos et al., 2012). Urbanicity may be a proxy for environmental risk factors more common to urban areas including social adversity (Heinz et al., 2013), greater prevalence of individuals of ethnic minority (Schofield et al., 2018) and greater exposure to air pollution (Attademo et al., 2017; Duan et al., 2018). Neighbourhood-level effects such as social fragmentation and deprivation have also been associated with increased risk of schizophrenia, though these are likely to be confounded, at least in part, by individual-level effects (Kirkbride et al., 2008; Kirkbride, Jones, Ullrich, & Coid, 2014; Solmi, Colman, Weeks, Lewis, & Kirkbride, 2017; Zammit et al., 2010).

Schizophrenia is a highly heritable disorder: based on recent estimates from a population registry data of twins in Denmark (N = 31,524 twin pairs; Hilker et al., 2018), the estimated heritability of schizophrenia is 79% and is similar for schizophrenia spectrum disorders (73%). The low concordance in monozygotic twins (0.33) highlights the importance of both shared and non-shared environmental (non-genetic) risk factors in the aetiology of schizophrenia. Genome-wide association studies using data from large consortia have identified over 100 independent genetic loci that are associated with schizophrenia at genome-wide levels of significance (Pardiñas et al., 2018). While individual loci have very small effects on risk, polygenic risk scores that index genetic risk en masse across the genome explain approximately 7% of schizophrenia heritability, and show that genetic liability to schizophrenia is distributed normally in the general population, which is consistent with a complex multifactorial aetiology and a continuum of psychosis expression (Gejman et al., 2010; Jones et al., 2016). In an umbrella meta-analysis, which analysed 41 meta-analyses of non-genetic risk factors for schizophrenia, obstetric complications, cannabis use, childhood adversities and stressful life events during childhood were identified as having the most robust associations with an increased risk of schizophrenia out of a total of 98 exposures (41 environmental factors and 57 biomarkers) analysed (Belbasis et al., 2018). These findings support the thesis that multiple environmental factors in both early life and during development contribute to an increased risk of schizophrenia.

Evidence of association between neurodevelopmental adversity and an increased risk of schizophrenia formed the basis of the neurodevelopmental hypothesis of schizophrenia first posited by Murray and Lewis (1987), which claimed that neurodevelopmental differences contributed to later onset of schizophrenia through changes in brain development (Jablensky, McNeil, & Morgan, 2017; Murray & Lewis, 1987). Evidence of an association between neurodevelopmental adversity and schizophrenia and psychosis-related outcomes have been observed in studies of prenatal infection, neonatal vitamin D deficiency, obstetric complications and maternal smoking (Brown and Derkits, 2010; Khandaker et al., 2013; Eyles et al., 2018; Niemelä et al., 2016; Quinn et al., 2017; Cannon et al., 2000; Giannopoulou et al., 2018; Dalman et al., 1999; Cannon et al., 2002; Fusar-Poli et al., 2017).

Consistent with the neurodevelopmental hypothesis, lower pre-morbid cognitive functioning is also associated with schizophrenia. Meta-analyses show that for every point reduction of IQ, the risk of subsequent schizophrenia is increased by 3.7% (95% CI: 3.4% - 3.7% p<.001) and that poorer cognitive functioning precedes schizophrenia onset (Dickson, Laurens, Cullen, & Hodgins, 2012; Khandaker, Barnett, White, & Jones, 2011). Evidence of an association between increased genetic risk of schizophrenia and lower IQ suggests that lower IQ may, in part, be a consequence of the increased genetic risk of schizophrenia (Hubbard et al., 2016). This neurodevelopmental model of schizophrenia has been subsequently expanded to accommodate evidence of the relationship between both exposure to drug use and other environmental factors over the life course (Murray, Bhavsar, Tripoli, & Howes, 2017). Studies of the association between viral infections and an increased risk of schizophrenia suggest that brain development can be affected through immune system activation and inflammation throughout early life (Khandaker et al., 2012; Allswede and Cannon, 2018).

This theory is also supported by GWAS findings which show that the strongest genetic signals for schizophrenia lie in the major histocompatibility complex region that controls immune function (Pouget et al., 2019).

There is also observational evidence from large cohort studies that supports the thesis that cannabis is a causal risk factor for schizophrenia (Moore et al., 2007; Zammit, Allebeck, Andreasson, Lundberg, & Lewis, 2002). Evidence of a causal relationship between cannabis use and schizophrenia is supported by mendelian randomisation analyses that can provide stronger evidence of causal inference than standard observational designs (Gage et al., 2017).

1.3.2 Non-affective psychotic disorders

Findings for other non-affective psychotic disorders generally reflect those for schizophrenia. However, the aetiology of affective psychotic disorders, such as bipolar disorder, shows some distinct differences. For example, while affective psychoses are also more common in urban than in rural areas, the within-city variation that is observed for non-affective disorders is absent, and evidence of neighbourhood-level effects is weaker for affective psychotic disorders (Kaymaz et al., 2006; Kirkbride et al., 2006). There is also weaker evidence to support a neurodevelopmental hypothesis for affective psychoses than for non-affective disorders. For example, evidence of impairment in pre-morbid cognitive ability is weaker and less consistent (Bora et al., 2010). This finding is despite the strong genetic correlation between bipolar disorder and schizophrenia, which suggests that similar biological mechanisms are likely to be involved in their aetiology and that both have a neurodevelopmental origin, even if they lie on different parts of a neurodevelopmental continuum (Owen & O’Donovan, 2017).

1.3.3 Sub-clinical symptoms of psychosis

Studies of environmental risk factors for PEs in the general population have reported similar findings as those for psychotic disorders as described above. Studies of prenatal risk factors have identified that maternal infection during pregnancy, maternal diabetes, low birth weight and maternal stress are associated with a greater likelihood of PEs in adulthood (Dreier et al., 2018; Spauwen, Krabbendam, Lieb, Wittchen, & Os, 2004; Thomas et al., 2009; Zammit et al., 2009). As with studies of schizophrenia, there is evidence that inflammation from infection during childhood and adolescence are associated with subsequent onset of PEs (Khandaker et al., 2014).

In early life, autistic traits (speech problems, unusual habits), other neurodevelopmental disorders (i.e. dyslexia, dyspraxia) and poor social and communication skills have been reported to be associated with a greater risk of subsequent PEs (Bevan Jones et al., 2012; Hameed et al., 2018; Khandaker et al., 2014). This is consistent with a neurodevelopmental account of the psychosis continuum and is supported by evidence that poorer cognitive functioning in childhood is associated with later PEs and PLEs (Barnett et al., 2012; Horwood et al., 2008). Genetic risk for schizophrenia may partly explain the relationship between lower IQ and PEs as there is evidence of shared genetic liability between PEs, schizophrenia and neurodevelopmental disorders (Legge et al., 2019).

There are environmental risk factors common to both schizophrenia and PEs, including sustained exposure to urban environments (Coid et al., 2018). Different characteristics more commonly found in urban environments that are associated with an increased risk of PEs and PLEs include exposure to air pollution, higher levels of crime victimisation and poorer social cohesion (Newbury et al., 2016; Newbury et al., 2019; Solmi et al., 2017). There is also evidence to support the hypothesis that cannabis use is causally associated with an increased risk of subsequent PEs (Gage et al., 2014; Jones et al., 2018).

Perhaps the main difference in the known aetiology of schizophrenia and sub-clinical symptoms of psychosis is in the distribution of both outcomes according to sex. While there is evidence that schizophrenia is more common in males, there is some evidence to suggest that sub-clinical symptoms are more common in females (Maric et al., 2003; McGrath et al., 2015), although this is not supported by meta-analyses (Linscott & Os, 2013; van Os et al., 2009).

As will be discussed below, there is also evidence to support the view that exposure to childhood trauma is associated with an increased risk of psychotic disorders and of sub-clinical psychotic symptoms. The current evidence base for the aetiology of psychotic outcomes across the psychosis spectrum suggests that there are similar risk factors for the development of both clinical and sub-clinical psychosis outcomes, indicating that studies of PEs can help to inform our understanding of the aetiology and development of more severe and clinical psychotic outcomes.

1.4 Childhood Trauma as a risk factor for psychosis

1.4.1 Epidemiology of childhood trauma

Throughout this thesis, I use the term childhood trauma to refer to experiences including abuse, victimisation or neglect of a severity that would likely cause substantial psychological distress in most people, and which occur before 18 years of age. This definition does not include instances of adversity such as economic adversity, parental drug use, parental mental illness and other negative life events that are often included in measures of stressors or adversity, such as the Adverse Childhood Experiences (ACE) study (Felitti et al., 1998).

1.4.1.1 The estimated prevalence of childhood trauma

There is a very wide range in estimations of the prevalence of exposure to trauma across studies; in a large meta-analysis (244 studies and 551 separate prevalence estimates), estimations ranged from 0-90% of individuals reporting exposure to trauma (Stoltenborgh et al., 2015). A large proportion of prevalence estimates are from investigations of sexual abuse, where estimates range from 13% in Europe to 20% in Africa (Stoltenborgh et al., 2015). Prevalence estimates for sexual abuse differ substantially according to sex: a global meta-analysis of 65 studies reported 19.7% of women and 7.9% of men report some form of sexual abuse before the age of 18 years (Pereda et al., 2009). The prevalence of physical abuse ranges from 4%-19%, emotional abuse 11%-46% and neglect 14%-30% according to estimates from different continents (Stoltenborgh et al., 2015). Estimates of exposure to multiple types of trauma range from 20% to 70.5% (Copeland et al., 2018; Finkelhor et al., 2009; Saunders & Adams, 2014).

1.4.1.2 Variation in prevalence estimates of childhood trauma exposure

Prevalence estimations vary greatly according to the type of trauma recorded, the methodology used (e.g. measuring a single type of trauma or a range of trauma types), the timing of trauma that is asked about (e.g. lifetime vs past year) and severity of the exposure. Methodological considerations play a substantial role in the heterogeneity of prevalence estimates; informant-reported trauma is lower than self-reported exposure to trauma. Differences in how trauma is assessed, be it by using parent-reported data, questionnaire or interview, and how different types of trauma are defined can vary substantially across studies.

A recent meta-analysis by Baldwin and colleagues (2019) identified that the timing of trauma assessment and methodology of assessment plays an important role in the likelihood of a disclosure. In the meta-analysis of 16 studies that assessed exposure to trauma at multiple timepoints, 52% of participants who reported trauma during a first assessment did not report the exposure at a later time-point. The agreement between reporting at different timepoints was greater in studies that used interview assessment compared to questionnaire data. Differences in reporting may also be due to memory biases, false disclosure or nondisclosure at either of the timepoints.

1.4.1.3 Childhood trauma and the risk of subsequent re-victimisation

Exposure to trauma is associated with an increased risk of subsequent interpersonal violence in adolescence and adulthood (Fisher et al., 2015; Lurie, Boaz, & Golan, 2013; Radford, Corral, Bradley, & Fisher, 2013; Shevlin et al., 2013), which in turn further increases the risk of psychopathology and other negative health outcomes. Exposure to abuse in different settings during both childhood and adulthood is associated with a greater likelihood of complex negative mental health and negative social outcomes compared to exposure to a single type of trauma (Banyard, Williams, & Siegel, 2001; Briere, Kaltman, & Green, 2008; Menard, Bandeen-Roche, & Chilcoat, 2004).

1.4.2 Childhood trauma and psychosis-related outcomes

Meta-analyses have observed a relationship between exposure to childhood trauma and a 2-3 fold increased risk of psychotic outcomes across the psychosis continuum (Bailey et al., 2018; Cancel et al., 2016; Cunningham et al., 2016; Dam et al., 2012; Gibson et al., 2016; Morgan and Gayer-Anderson, 2016; Trotta et al., 2015; Varese et al., 2012). These findings are based on case-control, cross-sectional and cohort study designs in clinical and general population samples. The population attributable risk (PAR) of exposure to trauma on psychosis outcomes, based on the assumption that the relationship is causal and estimated correctly, is 33% (95% CI 16% - 47%; Varese et al., 2012).

The prevalence of trauma exposure is significantly higher in individuals at ultra-high risk of psychotic disorder and those with a psychotic disorder, compared to general population controls (Corsi-Zuelli et al., 2019; Kraan et al., 2015; Larsson et al., 2013; Trauelsen et al., 2015). Based on meta-analytic estimates, the mean prevalence of exposure to trauma in individuals at ultra-high risk of psychosis is 87% (95% CI: 77%-93%), compared to exposure to trauma in control groups that ranged from 43%-60% (Kraan et al., 2015). Trauma is also associated with greater psychotic symptom severity in clinical groups (Dam et al., 2015; Mansueto et al., 2018). In general population samples, childhood trauma is associated with an increased risk of both PEs and PLEs (Cunningham et al., 2016; Trotta et al., 2015; Varese et al., 2012).

1.4.2.1 Dose-response relationship between trauma and PEs

The Bradford-hill criteria state that an observed association is more likely to be causal if 'the outcome increases monotonically with increasing dose of exposure' (Hill, 1965). Several studies have observed a dose-response relationship between the number of different types of trauma exposure reported and an increase in the risk of PEs or PLEs (Arseneault et al., 2011; Bentall et al., 2012; De Loore et al., 2007; McGrath et al., 2017; Moriyama et al., 2018; Shevlin et al., 2008; Lataster et al., 2006). Frequency of single type of trauma also shows a dose-response association with symptoms of psychosis across the continuum (Mackie et al., 2013; Shevlin et al., 2013; Trauelsen et al., 2015). A dose-response relationship between the number of traumatic stressors reported and the severity of psychotic symptoms in clinical populations has also been reported (Longden et al., 2016; Muenzenmaier et al., 2015).

1.4.1.2 The role of trauma type on psychosis-related outcomes

There is evidence to suggest that different types of trauma may vary in the extent to which they increase the risk of psychosis-related outcomes. It has been observed that exposure to accidental injury and the loss of a parent or sibling are less likely to be associated with PEs compared to interpersonal violence or neglect (Arseneault et al., 2011; McGrath et al., 2017; Moriyama et al., 2018; Spauwen et al., 2006; van Nierop et al., 2014). However, a recent large case-control study has reported evidence that early death of either a mother or both parents is associated with an increased risk of a first episode of psychosis (Misra et al., 2019).

It is currently unclear whether different types of inter-personal violence and neglect have differential effects on risk of psychotic symptoms. Several studies have examined a single type of trauma (Bebbington et al., 2011; Schreier et al., 2009; Wolke, Lereya, Fisher, Lewis, & Zammit, 2014), and provide evidence to support the thesis that specific types of interpersonal violence are each associated with risk of psychotic symptoms or PEs but does not allow a comparison between trauma types in the same sample. In studies that analysed multiple types of trauma, the estimated effect size for exposure to sexual abuse on the risk of psychosis-related outcomes was greater than the effect size from exposure to bullying and physical abuse (Bebbington et al., 2004; Bell, Foulds, Horwood, Mulder, & Boden, 2019; De Loore et al., 2007). However, the confidence intervals for these estimates overlapped, therefore providing little evidence to suggest that the effects of sexual abuse on the risk of psychosis-related outcomes are greater than other types of trauma.

One difficulty with determining whether different types of trauma are independently associated with risk of PEs is that exposure to different trauma types frequently co-occurs, which may introduce collinearity into estimation models. McGrath and colleagues (2017) used multivariable regression modelling to adjust for exposure to other types of trauma in a single model. In this analysis of cross-sectional data, rape was associated with the highest increase in the likelihood of PEs; however, confidence intervals with other trauma types overlapped, therefore providing little evidence of differential effects of trauma types.

In a clinical study that used penalised regression modelling, which controls for collinearity between different exposures, neglect was identified as the trauma exposure associated with the greatest increase in severity of psychotic symptoms (Schalinski et al., 2017). In another study, however, physical abuse perpetrated by mothers had the strongest association with an increased likelihood of psychotic disorder when adjusting for other trauma exposures, though confidence intervals for all effect estimates overlapped (Fisher et al., 2010).

Overall, studies provide evidence to support the view that different types of interpersonal violence and neglect are strongly associated with an increased risk of psychosis-related outcomes across the psychosis continuum. However, few studies have compared different types of trauma exposure and the risk of PEs in a single model; this limits the current inferences that can be made about whether a specific type of trauma differentially increases the risk of subsequent PEs.

1.4.1.3 Are types of trauma exposure associated with specific psychotic symptoms?

Some cross-sectional and longitudinal studies have also investigated whether different types of trauma are more likely to increase the risk of specific symptoms of psychosis (hallucinations, delusions) to establish whether there may be different aetiological pathways for different psychosis-related outcomes.

Based on cross-sectional data from the Adult Psychiatric Morbidity Survey (n=7,353; Bentall et al., 2012), there was some evidence to suggest that rape was associated with self-reported hallucinations (OR=6.09; 95% CI: 1.38-26.89), but less evidence to suggest that there was an association between rape and self-reported symptoms of paranoia (OR=1.29 95% CI: 0.38 – 4.41). Bentall and colleagues (2012) report a lack of evidence for a relationship between exposures to sexual trauma that do not involve rape (sexual talk, sexual touch) and PLEs. In cohort studies, discussed later in this section, sexual abuse substantiated by local authorities was not found to be associated with an increased risk of different self-reported psychotic symptoms (Abajobir et al., 2017), whereas self-reported sexual abuse was reported to be strongly associated with different sub-clinical psychotic symptoms assessed by both self-report and interview (van Nierop et al., 2014). Based on the limited number of studies that have investigated the differential effects of trauma type on specific sub-clinical symptoms, a substantial overlap in confidence intervals between effect estimates of different types of trauma and wide confidence intervals for estimated effects, there is inconsistent evidence to suggest that there are differential effects on the risk of psychotic symptoms according to trauma type.

1.4.1.4 Timing of trauma and psychosis-related outcomes

Along with trauma type, the timing of trauma exposure during development may play an important role in determining the extent to which trauma increases the risk of psychotic outcomes. There is evidence from animal studies and human studies that exposure to stress affects brain development differently according to the timing of exposure, which is likely due to the maturation of different brain regions during stages of development (Schroeder et al., 2018). Consequently, stress at different developmental periods is hypothesised to differentially increase the likelihood of psychopathology (Lupien et al., 2009). In human studies, mid-childhood has been identified as a period where exposure to maltreatment is associated with poorer emotional regulation and an increased risk of depression in adulthood compared to exposure to maltreatment during other developmental periods (Andersen and Teicher, 2008; Dunn et al., 2018). These findings may have implications for the relationship between trauma timing and the development of psychotic symptoms.

In a study that analysed exposure to trauma that had occurred during different age-periods as separate exposures, the effect sizes for exposure to bullying and physical abuse before age seven years on PLEs was similar to that for exposure between age 7-12 years (Arseneault et al., 2011). Spauwen and colleagues (2006) also reported that exposure to multiple types of trauma before age 12 years and after age 13 years had overlapping confidence intervals for PLEs risk.

1.4.1.5 Is the association between childhood trauma and psychosis-related outcomes causal?

While studies show consistent evidence of an association between exposure to childhood trauma and psychotic outcomes, an essential requirement for increasing our understanding of psychosis aetiology and for the development of interventions to prevent the onset of psychotic experiences is whether this association is causal effect. As illustrated by results from Varese and colleagues' (2012) meta-analysis, a substantial proportion of studies of trauma and psychotic symptoms are cross-sectional and case-control designs, which limit the causal inferences that can be made from the evidence due to the possibility of reverse causality or, especially for case-control studies, selection bias.

Longitudinal studies of the relationship between trauma and psychosis-related outcomes can provide more conclusive evidence about the potentially causal role between exposure to trauma and the risk of subsequent PEs compared to cross-sectional and case-control study designs; cohort study designs minimise the risk of reverse causation by using data on an exposure that occurs before the outcome of interest. In the case of exposure to trauma during early or middle childhood and PEs, reverse causation is very unlikely due to timing of PEs onset later in development. The role of confounding can also be investigated more robustly in longitudinal study designs by testing potential confounders that are temporally prior to both the exposure and outcome. The extent to which previous studies address the contribution of confounding to observed effect estimates will be discussed.

1.4.1.6 Longitudinal studies of childhood trauma and psychotic experiences

Several cohort studies have investigated the association between exposure to childhood trauma and subsequent PEs and PLEs. Pooled analysis of 8 cohort studies by Varese and colleagues (2012) estimates that exposure to trauma is associated with a 2.75-fold increase in the likelihood of psychotic symptoms (95% CI: 2.17 -3.47; Arseneault et al., 2011; Cutajar et al., 2010; De Loore et al., 2007; Janssen et al., 2004; Mäkikyrö et al., 1998; Schreier et al., 2009; Spauwen et al., 2006; Wigman et al., 2011). The estimated heterogeneity, indexed by the I^2 statistic, of the pooled analysis is 67%, which suggests that heterogeneity is moderate (Higgins & Thompson, 2002). Two studies in the pooled analysis included the null value in the confidence intervals (Mäkikyrö et al., 1998; Spauwen et al., 2006), both of which included measures of trauma exposure types (death of a parent, accidental injury) that are less consistently associated with PEs compared to interpersonal violence or neglect (McGrath et al., 2017).

In a pooled analysis of 7 cohort studies of exposure to bullying (between ages five years to age 15 years; follow-up between 2-10 years), there was an estimated 2.15-times increase in the risk of subsequent psychosis-related outcomes (PLEs, PEs and confirmed psychotic disorder; Cunningham et al., 2016). The single study in the pooled analysis that did not detect an association between bullying and increased risk of psychotic symptoms assessed bullying using a single question (“Have you experienced bullying at or on your way to school?”; Bratlien et al., 2014) and assessed confirmed psychotic disorder at a seven-year follow-up (n=30). Both the use of a single question relating to bullying, which does not assess recency or severity and the rare outcome of confirmed psychotic disorder compared to other studies in the pooled analysis of sub-clinical psychotic symptoms are likely to have contributed to a reduced likelihood of detecting an association between bullying and psychotic symptoms in this study.

In a large cohort study published after the two meta-analyses of trauma and psychosis-related outcomes, exposure to different types of interpersonal violence and neglect at age 14 years (n=167, 4.5%), was associated with an increased likelihood self-reported symptoms of PLEs - defined as being in the top decile of the Peter's Delusion Inventory self-report scale (9.5%; n=353) - at approximately age 20 years (ORs 2.31 to 3.78; Abajobir et al., 2017).

These findings illustrate that the majority of longitudinal studies do report a strong association between exposure to trauma and an increased risk of PEs or PLEs. However, as discussed in the previous section, there are currently limitations in what is known about confounding and the differential effect of trauma type and timing on the risk of PEs.

1.4.1.7 Confounding

It is plausible that there are characteristics associated with both exposure to trauma and psychotic experiences that lead to an observed association. Potential sources of confounding are likely to be related to indices of deprivation and adversity (parental drug use, parental mental health difficulties) and lower socio-economic status in early life (Brown et al., 1998; Chaffin et al., 1996). Further to this, there is some evidence that an increased genetic risk of psychopathology is associated with an increased risk of exposure to trauma (Leppert et al., 2019; Schoeler et al., 2019; Winkel et al., 2013), and hence may confound the association between trauma and psychosis-related outcomes.

The majority of studies do adjust for potential confounders; however, what variables are selected vary across studies which makes the extent of attenuation from confounders unclear.

Inferences about confounding are limited as some studies do not adjust for any confounding variables (Kelleher et al., 2013) or only report adjusted results, which does not provide insight into the extent to which confounders attenuate unadjusted effect sizes estimates (Bell et al., 2019). As will be discussed later in the section, there are several studies that potentially over-adjust for variables that may mediate, rather than confound, estimations. In this case, over-adjustment for variables that are not suitable confounders may bias reported results.

In a sensitivity analysis of pooled studies, the increase in odds of psychotic symptoms for those exposed to trauma remained similar (2-3 fold) when restricted to studies that controlled for age, sex and socio-economic status (Varese et al., 2012). Fewer studies, discussed below, have examined indices of genetic risk for schizophrenia as a potential confounder.

In the studies that report both unadjusted and adjusted estimates, results suggest that confounders attenuate the association between trauma and PEs. However, they do not entirely account for observed associations (Arseneault et al., 2011; De Loore et al., 2007; Spauwen et al., 2006). Arsenault and colleagues (2011) reported that adjustment for IQ, socio-economic status and sex attenuated the association of exposure to maltreatment and bullying and the risk of PEs by between approximately 15%-20%. The study separately adjusted for childhood psychopathology (approximately 7%-19% attenuation) and genetic risk of PEs (approximately 14%-31% attenuation). These results suggest that genetic risk, psychopathology and socio-economic status may well confound the association between exposure to trauma and PEs, but that the association between exposure to bullying, intentional harm and subsequent PEs is still observable after adjustment (adjusted ORs 2.12 – 4.04). However, adjustment for all confounders (socio-economic status, psychopathology, and genetic risk) in a single model is not reported in the study. Therefore, it is unclear whether the association between childhood trauma and PEs would be observable after adjusting for all measured confounders.

De Loore and colleagues (2007) reported that the association between sexual abuse between ages 14-18 years old and PLEs between 5-34 months later was attenuated by approximately 24.9% after adjustment for confounders (age at baseline, sex, the timing of assessment and education level) but remains strongly associated with PLEs.

Several studies have investigated whether markers of increased genetic risk of psychosis attenuate the association between trauma and psychotic symptoms. There has been little evidence to suggest that controlling for genetic risk of psychosis substantially attenuates the association between trauma and PEs from twin study designs (Arseneault et al., 2011; Lecei et al., 2019), or comparisons of individuals with psychotic disorder, their siblings and population controls (Dam et al., 2015; Heins et al., 2011).

Some studies have identified factors as potential confounders that are more likely to mediate the relationship between exposure to trauma to an increased likelihood of PLEs, including cannabis use, mental health disorders at follow-up and chronic stress (Abajobir et al., 2017; Bell et al., 2019; Lataster, Myin-Germeys, Lieb, Wittchen, & Os, 2012; Spauwen et al., 2006). The occurrence of these factors is likely to occur after exposure to trauma and contribute to an increased likelihood of PEs. In studies that have adjusted for these potential mediators as well as potential confounders, estimated effect sizes have been attenuated by between approximately 19% - 41% and, in several cases, the association between trauma and psychotic symptoms is no longer observable (Abajobir et al., 2017; Lataster et al., 2012; Spauwen et al., 2006). As these studies adjust both potential confounders (i.e. socio-economic status) and potential mediators in a single model, the extent to which potential confounders attenuate this association is unclear. It is likely that inappropriately adjusting for variables as confounders that are more likely to be potential mediators biases results; this leads to an underestimation of the true causal effect of trauma on the risk of psychosis-related outcomes.

Overall, results from studies that have adjusted for confounders do not suggest that confounders explain the observed association between exposure to trauma and subsequent PEs. However, there may be residual confounding in reported results due to some studies not adequately controlling for increased genetic risk of psychosis, family history of psychopathology, or indices of social adversity.

1.4.3 The significance of childhood trauma

Exposure to trauma is associated with a greater likelihood of developing psychotic disorders, but also of other negative mental health outcomes including PTSD, anxiety, depression, substance misuse and personality disorder (Alisic et al., 2014; Kisely et al., 2018; Lewis et al., 2019; Norman et al., 2012). There is also evidence that exposure to forms of interpersonal violence and neglect during childhood is associated with adverse physical health outcomes including a greater risk of cardiac arrest, inflammation and type 2 diabetes (Baumeister et al., 2016; Goodwin & Stein, 2004; Huang et al., 2015).

As a large proportion of the global population is exposed to trauma during childhood, trauma is a public health issue that carries a substantial societal and economic burden (Fang et al. 2012; Ferrara 2015). Identifying risk factors for exposure to trauma and possible interventions are of paramount importance to reduce the risk of developing subsequent health difficulties. However, preventing exposure to childhood trauma is not easily achievable, and therefore identifying potentially modifiable mechanisms that mediate the pathways from exposure to trauma to negative health outcomes may provide opportunities to develop interventions that mitigate the long-lasting consequences of childhood trauma on health outcomes.

1.5 Potential mediating mechanisms between trauma and psychosis-related outcomes

Based on the hypothesis that trauma has a causal relationship with an increased risk of PEs, several studies have investigated the potential mediators of this relationship. As is discussed in section 1.4.1.7, evidence that adjustment for potential mediators (drug use, cannabis use, later mental health disorders and chronic stress) substantially attenuates the association between trauma and sub-clinical psychotic symptoms may provide support for their role on the pathway from trauma to PEs or PLEs. A recent systematic review of potential psychological mediators (Williams et al., 2018) between exposure to trauma and PEs identified mediators including symptoms of non-psychotic psychopathology (PTSD, anxiety and depression), poor emotional regulation, attachment style, low self-esteem and drug use.

However, there are significant limitations to the evidence base for mediators on the pathway from exposure to trauma and psychotic symptoms. As mediation analysis assumes a causal relationship between an exposure and outcome, then mediation estimate will be biased if the trauma to PEs effect-estimate is an over- or under-estimate of the true causal effect. As discussed by Williams and colleagues (2018), the current evidence base is limited by the cross-sectional data used in a large proportion of studies and a lack of adjustment for confounders on the pathway from trauma to psychosis-related outcomes.

As exposure to trauma is associated with a wide range of negative mental health outcomes and PEs/PLEs are commonly associated with co-morbid mental health problems, it has been hypothesised that non-psychotic psychopathology may mediate the association between trauma and psychotic outcomes. There is some evidence, from cross-sectional studies, that PTSD symptoms mediate the relationship between childhood trauma and psychotic symptoms by approximately 45% (Choi et al., 2015). In studies that have used longitudinal data from the ALSPAC cohort, exposure to early life stressors (bullying and harsh parenting) and subsequent PEs was partially mediated (approximately 30%) by symptoms of anxiety and depression (Fisher et al., 2013). It is not clear whether symptoms of depression, anxiety or PTSD overlap and co-occur with symptoms of psychosis or whether non-psychotic psychiatric symptoms precede psychotic symptoms and contribute to their aetiology. In a clinical sample, network analyses of childhood exposure and multiple mental health outcomes suggests that there is no direct relationship between trauma and psychotic symptoms but that different types of trauma exposure increase the risk of different symptoms of poor mental health that, in turn, contribute to the increased risk of PEs (Isvoranu et al., 2017).

It has been hypothesised that exposure to trauma leads to an increased risk of depression, anxiety and psychotic disorders via a shared pathway of dysregulated responses to stress (Williams et al., 2018). Exposure to trauma is associated with poorer emotional regulation and increased self-reported sensitivity to stress in everyday situations (Dunn, Nishimi, et al., 2018; Lardinois et al., 2011; van Nierop et al., 2018). Exposure to trauma is also associated with biomarkers that signify increased responses to stress including cortisol reactivity (Cicchetti et al., 2010; Knack et al., 2011; Saridjan et al., 2010) and C-reactive protein levels (Baumeister et al., 2016; Chase et al., 2019). However, a small number of longitudinal studies that have examined this have not found strong evidence that the association between trauma and PEs is mediated by emotion regulation (Bak et al., 2005; Lincoln, Marin, & Jaya, 2017; Thompson et al., 2013).

At a psychological level of explanation, it has been suggested that experiences of environmental stressors, including traumatic stress, elicit feelings of social defeat. Social defeat refers to chronic feelings of outsider status and is associated with negative mental health outcomes (Björkqvist, 2001). Animal studies have reported that experiences of social defeat are associated with biological markers of stress, including inflammation and increased dopaminergic activation (Selten et al., 2013; Toyoda, 2017). The social defeat hypothesis argues that different stressors can lead to an increased risk of psychotic symptoms by engendering feelings of social defeat (Selten et al., 2013; Selten and Cantor-Graae, 2005). This concept could explain why trauma exposures that involve victimisation and neglect are more strongly associated with risk of psychotic symptoms compared to stressors that are less likely to involve social exclusion (e.g. accidental injury). A study using cross-sectional data measured social defeat, based on participants' attitudes towards the future and their self-efficacy, and reported that social defeat accounted for a large proportion of the effect (86%) between exposure to childhood trauma and increased risk of PEs in a mediation model (van Nierop et al., 2014).

It is also hypothesised that exposure to trauma increases the likelihood of negative beliefs about the self and others (negative cognitive schema), which in turn leads to an increased risk of psychotic-related outcomes (Birchwood, 2003; Garety et al., 2001). In a case-control sample of participants at ultra-high risk of psychotic disorder, negative cognitive schema about the self partially mediated the relationship (14.7%) between emotional neglect during childhood and risk of psychotic disorder (Appiah-Kusi et al., 2017). In a general population sample (n=212), anxiety and negative self-schemas accounted for 45% of the association between emotional abuse and PLEs (Fisher, Appiah-Kusi, & Grant, 2012).

As discussed, cannabis use has been identified as a causal factor for the development of symptoms of psychosis. Several studies have investigated whether exposure to trauma may increase the likelihood of cannabis use and whether cannabis is a mediator between trauma and psychotic-related outcomes. Findings from two large general population studies provide little evidence to support the hypothesis that cannabis use mediates the relationship between trauma and PEs/PLEs (Bebbington et al., 2011; van Nierop et al., 2014). However, both studies were assessed as being of poor quality in the systematic review by Williams and colleagues (2018) due to a lack of robust mediation methods and validated measures of trauma exposure and cannabis use.

As will be outlined in the next chapter, it is also hypothesised that potentially modifiable information-processing biases could mediate the relationship between exposure to trauma and psychosis-related outcomes. There is evidence that biases in probabilistic inference (e.g. decision making, estimating the odds of an outcome) are associated with an increased likelihood of psychotic symptoms, and theoretical models suggest that these biases mediate the relationship between trauma and psychotic symptoms (Garety et al., 2001; Howes & Kapur, 2009). However, as will discussed, the relationship between exposure to trauma and information-processing biases has been largely unexplored.

1.6 Remaining questions about the relationship between trauma and PEs

In summary, the studies reviewed provide strong evidence for an association between exposure to trauma and an increased risk of psychotic outcomes in clinical and sub-clinical groups. However, several questions remained unresolved concerning the relationship between trauma and PEs at the time of starting the projects included in this thesis.

As discussed, there are potential sources of non-casual associations that may contribute to the observed association between trauma and PEs that require further investigation. The extent to which confounders attenuate the relationship is unclear due to inconsistencies in the approach to selecting potential confounders and reporting both unadjusted and adjusted results. Gaining a better understanding of the extent to which the relationship between childhood trauma and an increased risk of PEs is attenuated when rigorously controlling for both genetic and environmental confounders will provide greater insight into this relationship. It will also address the possibility of residual confounding that may be present in previous studies that have not controlled for both environmental and genetic risk factors in a single model.

Further to questions regarding causality, it is not known whether the relationship between trauma exposure and PEs differs according to the timing or type of interpersonal violence or neglect reported. Few studies have examined whether there is a sensitive or critical period of development where exposure to trauma may be associated with the greatest risk of trauma by analysing exposure to trauma at multiple timepoints. Establishing if critical or sensitive periods exist can give a greater insight into the pathway to PEs and potentially inform intervention strategies. Further research is also needed to establish whether there is a specific relationship between a specific type of trauma exposure and a greater risk of PEs. The studies reviewed in this chapter report overlapping confidence intervals between different types of trauma, but few have used multivariable regression modelling to control for the effects of different types of trauma exposure: this approach may provide more definitive answers about the potential independent effects of exposure to different types of trauma and provide greater insight into what aspects of trauma may be specifically associated with the development of PEs.

Establishing the direction of causality between exposure to trauma and the development of PEs and gaining a more accurate estimate of the causal effect will aid the investigation of potential mechanisms that are on this causal pathway. Cohort studies of the relationship between trauma, potential psychological and biological mediators, and PEs have the potential to provide more definitive evidence of mechanisms that may be on the pathway from exposure to trauma and an increased risk of subsequent PEs.

Chapter 3. Introducing information-processing biases associated with psychosis

2.1 Introduction

As discussed in the previous chapter, if the relationship between exposure to trauma and psychosis is causal, it is important to establish what mechanisms lie on this pathway. These mechanisms may be targets of intervention and may occur on different levels of processing (e.g. biological, cognitive, psychological). Several theoretical frameworks suggest that abnormalities (biases) in information-processing are mechanisms on the pathway from trauma exposure to psychosis.

Broadly, information-processing biases refer to systematic differences in information processing compared to normative behaviour. Several different biases (e.g. hasty decision-making, overreliance on prior knowledge) are associated with psychosis in observational studies of clinical and general population samples and may be indicative of processes that contribute to the development of psychotic symptoms. In this chapter, I will introduce key theoretical models that aim to integrate different information-processing biases into a unified model of psychosis and review empirical studies of information-processing biases that are part of my systematic review (study II) and are tested using data from the ALSPAC cohort (study III).

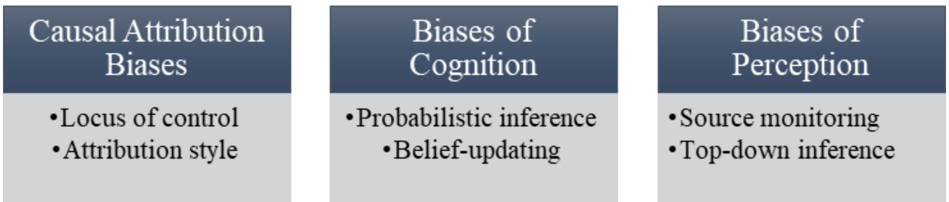
2.2 Information-processing biases

Information-processing biases are distinct from information-processing deficits. A deficit in information processing is indicated by poorer performance on a task, whereas a bias is a systematic difference from normative performance on a task. Impaired performance and biased performance on a task may be correlated but are not equivalent. As cognitive deficits are associated with psychosis, it is important to establish whether biases exist independently of such deficits or if poorer cognitive processing is a common cause of both cognitive biases and PEs.

An example of this distinction is observed in a task in which participants interpret emotions from a series of images of facial expressions. Individuals with psychosis show generally poorer performance in this task compared to controls (Kohler et al., 2010). In other words, they are worse in identifying any facial expression. Importantly, however, in addition to this generalised deficit in recognising emotions, individuals with psychotic symptoms are also biased towards identifying neutral and fearful faces as hostile (Premkumar et al., 2008). Both the deficit and the bias observed in performance on the task can have different implications for understanding psychosis: a generalised deficit in social cognition may result in increased difficulty in understanding emotions, whereas a bias towards perceiving hostility may result in a heightened sense of threat.

The biases reviewed in this section are classified into three broad categories: causal attribution, cognition, and perception (Figure 3.1). Causal attribution broadly refers to how individuals interpret the outcome of events in terms of agency and responsibility. For example, if an individual receives poor results in an exam, they may attribute the cause of this outcome to personal qualities such as not studying enough or revising the right material. In contrast, attributing the cause of the result to external events would include factors such as unusually difficult exam questions or punitive marking. Causal attribution biases are not tested empirically in the thesis but are included in the systematic review and meta-analysis (Chapter 6) and will be discussed briefly.

Figure 3.1 Summary of information-processing bias domains



Cognitive biases are examples of inference that may indicate that there are differences in how beliefs are updated. For example, if an individual makes a decision hastily in an inference task, this may indicate an underlying cognitive process where minimal evidence is needed to form a belief. A bias for hastily making decisions is referred to as the 'Jumping to Conclusions' bias (JTC) and will be discussed in-depth in section 2.4.2.

Perceptual biases are ways in which biased inference processes may influence how sensory information is perceived. One example of this is a bias for an overreliance on prior expectations when interpreting new information: this process may contribute to the development of abnormal perceptual experiences. Another example is a bias for identifying internally generated information (e.g. thoughts or speech) as coming from an external source (e.g. media or other people). This bias, referred to as an external source monitoring bias, is another example of how abnormal information-processing may be a mechanism that contributes to psychotic symptoms.

Empirical studies of information-processing biases associated with psychotic symptoms will be discussed in-depth in section 2.4.

2.3 Integrated models of psychosis

Theoretical models of psychosis aim to provide a unified account of how different processes contribute to the development of psychosis at biological, cognitive and psychological processes of explanation. I will first introduce cognitive models of psychosis, which focus on how biased cognitive processes may be triggered and exacerbated by environmental factors to contribute to the psychosis pathway. Following this, I will introduce the dopamine model of psychosis that integrates biological processes (e.g. hyperactivation of dopamine) with abnormal belief-updating processes. I will then conclude the section with the predictive processing model of psychosis that focuses on how different information-processing biases associated with psychosis may be due to abnormal belief-updating. Each model illustrates how the association between abnormal belief-updating processes and psychosis can inform hypotheses about mechanisms on the theorised causal pathway from exposure to traumatic stress to the development of psychosis.

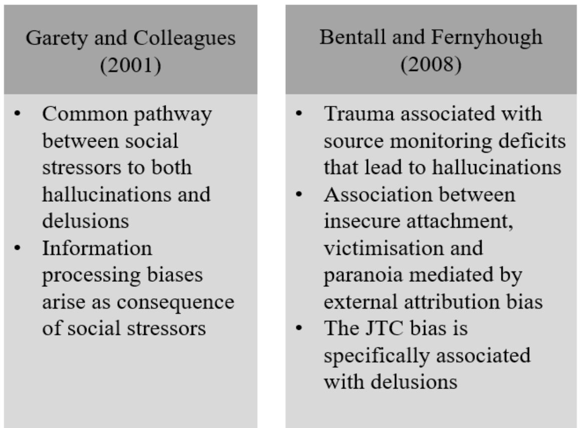
3.3.1 Cognitive models of psychosis

Cognitive models of psychosis that aim to understand the JTC bias and self-monitoring deficits were proposed by Garety and colleagues (Garety et al., 2001; Kuipers et al., 2006) and later by Bentall and Fernyhough (2008). These models theorise that information processing biases lie on the pathway from environmental exposures to the development of psychotic symptoms.

In Garety and colleagues' model, a prior vulnerability to psychotic symptoms is aggravated by environmental stressors including adversity, isolation and drug use. These environmental stressors are theorised to 'weaken' perceptual faculties such as source monitoring and increase the likelihood of memory intrusions, which may make an individual's actions seem uncontrollable and alien. These processes are thought to occur during the prodromal stage in the development of a psychotic disorder, where perception becomes increasingly abnormal, but psychotic symptoms are not yet established. The emotional responses to these cognitive changes are understood to influence the interpretation and content of these experiences. For example, if these experiences are distressing, an individual may be more prone to attribute external malevolent causes to explain their occurrence. Information-processing biases are modelled as the consequence of environmental stressors and as a mechanism that contributes to the development of both hallucinations and delusions. In this account, individuals who are more isolated and less likely to question whether their abnormal perceptions are irregular are at greater risk of psychotic symptoms, whereas social protective factors could ameliorate this risk.

Bentall and Fernyhough's (2008) cognitive model similarly supports the role of trauma in the psychosis pathway but suggests a specificity between different biases and symptoms. The association between exposure to trauma, particularly sexual abuse, and an increased risk of hallucinations is theorised to be mediated by source monitoring deficits that are caused by intrusive traumatic memories. In contrast, paranoia is modelled as the consequence of insecure attachment and victimisation in early life, which in turn lead to external attribution biases and the JTC bias. In this model, the JTC bias is theorised only to be associated with delusions, not hallucinations, and to contribute to the maintenance of paranoid beliefs once they are established.

Figure 3.2 Summary of cognitive models of psychosis discussed in this chapter



These models (Figure 2.2) illustrate how evidence of the association between information processing biases and psychotic symptoms can be interpreted in theoretical models of psychosis. Where Garety and colleagues state that information-processing biases occur along a single pathway from environmental triggers to symptoms of both hallucinations and delusions, Bentall and Fernyhough propose that environmental factors do not necessarily trigger specific information-processing biases that contribute to different symptom outcomes.

As will be reviewed in section 3.4.2, few studies have examined the potential specificity between different information-processing biases and psychotic symptoms that can inform these models. Further to this, the relationship between social stressors and information-processing biases is currently unclear, but these models provide theoretical support for a relationship between exposure to traumatic stress and information-processing biases associated with psychosis.

3.3.2 The dopamine model of psychosis: aberrant salience

The relationship between dopamine dysregulation and schizophrenia has been central to schizophrenia research since the discovery of the efficacy of antipsychotic drugs that block dopamine receptors (Kapur & Mamo, 2003; Seeman et al., 1976). Subsequent research has focused on the relationship between psychotic symptoms as a dimension within both schizophrenia and other psychiatric disorders and hyperactivation of dopamine in the mesolimbic pathway (Davis et al., 1991). This approach is supported by findings of the association between dopamine hyperactivity and psychotic phenomena across the spectrum of psychosis symptom severity (Egerton et al., 2013; Mohr & Ettinger, 2014), and with symptoms of psychosis that occur outside the context of schizophrenia (Jauhar et al., 2017).

Howes and Kapur suggest that multiple routes from genetic, neuro-developmental and environmental risk factors for psychosis contribute to increased dopamine activation. It is also established that exposure to environmental stressors is associated with altered dopamine activation activity (Hall et al., 1999, 1998; Mittal et al., 2013; Prabhu et al., 2018; Seeman et al., 2005; Winkel et al., 2013). This evidence suggests that dopamine activity is a mediator between exposure to stress and the subsequent risk of psychotic symptoms.

In considering how dopamine hyperactivity may be manifest in abnormal inferential processes, Howes and Kapur propose that dopamine hyperactivity alters how salience is attributed to features of an environment. When functioning regularly, dopamine is thought to help differentiate relevant stimuli (salient) from irrelevant (non-salient) stimuli: a process integral to making accurate predictions about, and perceiving, environmental stimuli (Kapur, 2003). Attributing salience directs attention to stimuli and contributes to the formation of reliable predictions about future events. Correct attribution of salience is a mechanism involved in areas of cognitive processing associated with dopamine function, including reinforcement learning (Bromberg-Martin et al., 2010) and regulating goal-driven behaviour (Berridge, 2012).

Information processing becomes dysregulated as salience is attributed to irrelevant stimuli, which Kapur (2003) describes as a gradual process occurring during the prodromal phase of psychosis development, where sensory information is interpreted as having a hidden meaning or excessive profundity and contributes to a 'delusional atmosphere' (Bowers & Freedman, 1966; Møller, 2000). In this phase, the aberrant salience process leads to chaotic attributions of meaning and abnormal inferential processes that could lead to distressing or bizarre experiences, including paranoia and abnormal perceptions.

2.3.2.1 Empirical studies of aberrant salience

Few studies have examined whether aberrant salience is more commonly observed in individuals with increased dopamine activation or psychotic symptoms. An association between increased attribution of meaning to irrelevant task stimuli in a salience attribution test (SAT) – a reinforcement learning paradigm that tests how well participants can assign value (salience) to stimuli and ignore irrelevant stimuli - has been associated with symptoms of schizophrenia, ultra-high risk states, and sub-clinical delusional ideation (Katthagen et al., 2016, 2018; Roiser et al., 2013).

In line with Howes and Kapur's model, aberrant salience has been reported to be associated with elevated presynaptic dopamine levels in a general population sample (Boehme et al., 2015). Aberrant salience is also associated with poorer adaptive learning, slower cognitive processing and impaired reversal learning (Boehme et al., 2015; Katthagen et al., 2016), which may suggest that aberrant salience is related to a range of different cognitive processes, including information-processing biases. There is also some evidence that environmental risk factors for psychosis (cannabis, chronic social stressors) are associated with a greater likelihood of attributing meaning to irrelevant stimuli in SAT tasks (Bloomfield et al., 2016; McCutcheon et al., 2018).

Findings of the relationship between aberrant salience, dopamine dysregulation and psychotic symptoms are limited by the few studies that have tested whether this association exists and whether it is not accounted for by confounding. It has also not been established whether aberrant salience is associated with information-processing biases associated with psychosis. Aberrant salience has been suggested as a mechanism that could contribute to abnormal belief-updating (Speechley et al., 2010), where contradictory evidence may seem excessively salient and inform beliefs more than information from consistent evidence.

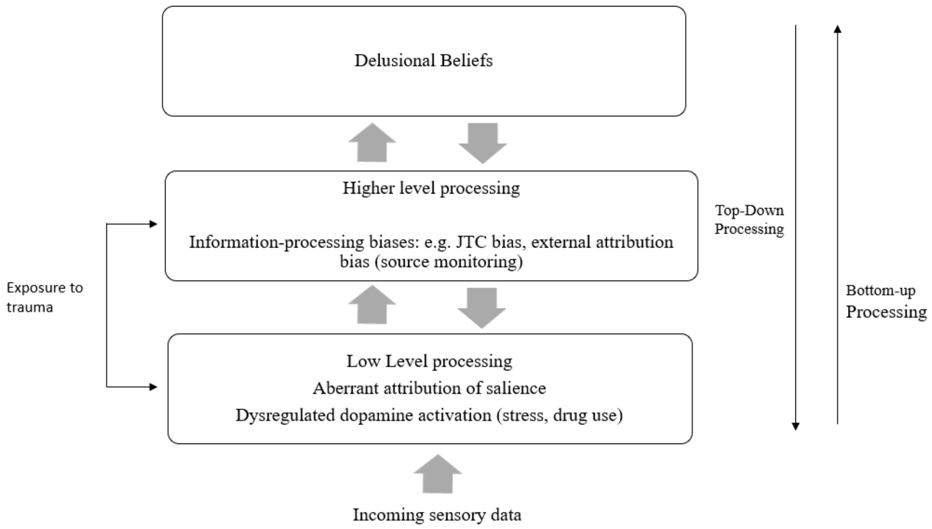
2.3.2.2 Integrating biases in a hierarchy of information-processing

In Broyd and colleague's (2017) model, information-processing biases and aberrant salience occur at different levels of an information processing hierarchy organised according to complexity (e.g. immediate sensory perception at the bottom, development of complex beliefs at higher levels of processing; Figure 2.3).These levels interact with one another and are influenced by dysregulated dopamine.

At the lower level of the processing hierarchy, how attention is allocated is dysregulated (aberrant salience) in psychosis by abnormal dopamine activation; this means that irrelevant features of an environment are interpreted as unusually significant and potentially threatening. Environmental factors such as drug use and exposure to trauma contribute to aberrant salience, which then interacts with higher levels of the processing hierarchy.

At the higher level of the hierarchy, more complex beliefs (e.g. global beliefs, social judgements) are influenced by information-processing from the lower level of the processing hierarchy. Biased information-processing at lower levels of the processing hierarchy (e.g. misperception of sensory data as threatening) contribute to the formation of abnormal complex beliefs at higher levels (e.g. persecutory delusions). Both levels of processing are also influenced by trauma and other social factors, which can inform the content of irrational beliefs. Different levels of the information-processing hierarchy interact bidirectionally: higher-order ideas inform how salience is allocated in lower levels of information processing. This model accounts for how exposure to trauma (i) may increase sensitivity to stressors at lower levels of the hierarchy (e.g. responses to ambiguous sensory information) and (ii) may influence more complex processes that contribute to delusional beliefs (e.g. paranoid appraisal of social situations).

Figure 3.3 Summary of Broyd and colleague's (2017) integrated model of delusions



Overall, the dopamine model provides a framework to further describe how dopamine dysregulation may contribute to cognitive mechanisms that increase the risk of developing symptoms of psychosis. As Broyd's model illustrates, processes of belief-updating and allocation of attention occur at different levels of a cognitive processing hierarchy that, when dysregulated, contribute to the formation and content of delusional beliefs. This model provides theoretical support for the relationship between exposure to traumatic stress and information-processing biases on the psychosis pathway.

3.3.3 The predictive processing model of psychosis

The predictive processing model characterises the mind as a 'prediction machine' (Clark, 2013), which means that prediction is central to information processing and how an individual uses new information to respond and adapt to environments. This theory is based on the concept of 'unconscious inference' by von Helmholtz (1860) that claims that perception is a process that combines both prior expectations and new incoming sensory information that occurs outside of conscious awareness. Therefore, abnormal beliefs can influence perception and contribute to abnormal perceptual experiences.

For example, if I were to take a sip from a mug and sip coffee when I was expecting to taste peppermint tea, this would result in a prediction error: momentarily the taste of coffee would be jarring due to my contrary expectation. When I go to sip the drink again, the previous prediction error would inform a greater prior expectation of coffee: tasting the drink again would be consistent with my expectation. This prediction error drives belief-updating, and the sensation of taste in both instances will differ according to my expectation, illustrating how prior expectations are integral to how sensory data is perceived. In the predictive processing model of psychosis, the process of belief updating is hypothesised to be dysregulated, and that this increases the likelihood of psychotic symptoms (Fletcher & Frith, 2009; Sterzer, Adams, et al., 2018). If belief updating in response to prediction errors is dysregulated, this could lead to increased prediction errors and make the world seem continually surprising and unpredictable. In the case of psychosis, this consequent sense of unpredictability leads to the development of complex and irrational beliefs to account for these apparent inconsistencies.

For example, a chronic feeling that an environment is unpredictable may feel distressing and be best accounted for by the presence of a malevolent force, thus giving rise to paranoid delusions.

The predictive processing model suggests that different psychotic symptoms (i.e. hallucinations and delusions) are caused by a central abnormality in belief-updating. As predictive processing occurs at several levels of an information-processing hierarchy, alterations in predictive processing may have different effects on cognitive and perceptual domains (Sterzer, Adams, et al., 2018). In a study of perceptual inference, sub-clinical delusions were associated with both a poorer ability to stabilise sensory information from ambiguous stimuli (weaker lower-level expectations) and with biased beliefs about an outcome (stronger higher-level expectations; Schmack et al., 2013). These results illustrate how abnormal predictive processing can be manifest at different levels of an information-processing hierarchy and may contribute to the development of psychotic symptoms.

As will be discussed in section 2.4.3, processes involved in belief updating can be modelled mathematically using probability theory. By using computational frameworks to model behaviour based on theoretical principles, hypotheses informed by the predictive processing account of psychosis can be tested empirically. In the next section, I will review the current evidence base for the association between different information-processing biases and psychotic symptoms and discuss the implications of different models of psychosis.

2.4 Empirical studies of information-processing biases

3.4.1 Causal attribution biases

Attributing the cause of events to external forces such as other people or to chance, rather than internal factors such as personal action or character, is associated with poorer mental health outcomes. This relationship may be due to increased feelings of helplessness and reduced estimations of self-efficacy, contributing to the risk of mental health disorder. This bias is measured by two scales: locus of control (LOC) and attribution style. Both constructs use self-report measures to assess how individuals judge the cause of a series of hypothetical events. The LOC and the attribution style paradigms differ in what aspects of causal attribution they assess: the LOC measures causal attribution according to the extent to which a range of events are interpreted as caused by either external or internal forces, whereas attribution style measures causal attribution according to multiple characteristics (discussed below) for good and bad events separately.

2.4.1.1 Locus of control

The LOC scale measures the extent to which individuals believe that they have control over events in their lives. Those with a predominantly internal LOC believe that internal factors such as their personality traits and personal action are the main drivers of change in their lives. In contrast, those with a bias towards an external LOC are prone to identifying factors such as fate, chance, and luck to be the cause of events. A bias towards an external LOC is associated with a wide range of negative outcomes, including poorer educational attainment, impaired ability to cope with adverse circumstances, and poorer social cognitive ability (Nowicki, 2016).

Moreover, LOC is associated trans-diagnostically with both sub-clinical and clinical mental health outcomes: a more external LOC is observed in people with schizophrenia and in those with depression (Harrow et al., 2009). An external LOC in childhood is also associated with both PEs and depression in adolescence in a general population sample (Sullivan, Thompson, Kounali, Lewis, & Zammit, 2017; Thompson et al., 2011). A criticism of the LOC paradigm is that it is not used to assess LOC in positive and negative events separately. As LOC for positive and negative events are poorly correlated, this may indicate different biases within this construct (Brewin & Shapiro, 1984).

2.4.1.2 Attribution style

Attribution style measures how a cause is attributed to positive and negative events according to different dimensions (Kaney & Bentall, 1989). This measure, assessed using the Attribution Style Questionnaire (Peterson et al., 1982), assesses how global (generalisable rather than specific) and stable (persistent in the future) participant believe the cause of an event to be, as well as whether it is internal or external. Both increased attribution of global and stable factors to events are associated with an increased likelihood of depression and paranoia for both positive and negative events; whereas, as will be discussed, internal and external attribution biases differs for depression and psychosis (Kaney & Bentall, 1989; Pearson et al., 2015; Seligman & al, 1984; Sullivan, Bentall, Fernyhough, Pearson, & Zammit, 2013).

The contrast between depression and psychotic symptoms on the attribution scale is on external attribution bias for good and bad events: depression is associated with a tendency to attribute the cause of good events to external factors (Jolley et al., 2006; Martin & Penn, 2002), whereas individuals with psychotic disorder are more likely to attribute negative events to external factors (Janssen et al., 2006). However, the association between biased attribution of negative events to external factors has not been consistently reported across the psychosis spectrum. There is a lack of evidence to suggest an association between external attribution bias and an increased risk of PLEs (Janssen et al., 2006; Langdon, Still, Connors, Ward, & Catts, 2013; Martin & Penn, 2002) or PEs (Sullivan et al., 2013). These findings suggest that the association between external attribution bias and psychotic symptoms might only be observed in clinical populations. Qualitative analyses of attribution style in a sample of patients with delusional beliefs found that individuals expressed an externalising bias when discussing their delusions, whereas they expressed more internal attributions when referring to other negative events (Beese & Stratton, 2004). This qualitative analysis illustrates the complexity of understanding externalising attributions in relation to psychotic phenomena.

3.4.2 Biases in cognition

2.4.2.1 Probabilistic inference

There is evidence to suggest that abnormalities in how beliefs are formed and updated in response to new information are associated with an increased likelihood of psychotic symptoms. Perhaps the most tested bias in psychosis research is an observed tendency to make decisions more hastily and based on a smaller amount of information compared to controls. This bias, the ‘Jumping to Conclusions’ (JTC) bias, is thought to be a mechanism that contributes to delusional thoughts: if a person adopts new beliefs hastily and based on limited evidence, this may increase the likelihood of adopting irrational beliefs. The JTC bias has been observed in a widely used probabilistic inference task: the beads task (Phillips and Edwards 1966). In the ‘draws to decision’ version of the beads task, participants are presented with two jars of beads containing 100 beads of opposing ratios of two colours, typically 85:15. The experimenter then conceals the two jars and presents one bead (with replacement) from one of the jars: participants are asked to either decide which jar the bead is drawn from or request to see more beads from the same jar before they make this decision (for an illustration see Chapter 7). The number of beads that participants request before making that decision is the outcome of interest and referred to as the Draws to Decision (DTD).

The DTD outcome is interpreted as an index of how much information participants require before making a decision. In previous literature, a decision based on two or fewer beads has been classified as the JTC bias (Dudley, Taylor, Wickham, & Hutton, 2015; Garety et al., 2011). There are several variations of the beads task, which include the use of different ratios of coloured beads to vary task difficulty. The number of times that a participant completes the task can also vary across studies, with the JTC bias recorded as the value either from a single trial or as an average value from multiple trials.

2.4.2.2 Evidence of the 'Jumping to Conclusions' bias in clinical populations

In studies of clinical populations, an association between the JTC bias and diagnoses of schizophrenia or psychosis-related disorders has been widely observed. Several meta-analyses have reported an association between psychotic symptoms and a greater likelihood of displaying a lower average DTD or the JTC bias (Dudley et al., 2015; Fine et al., 2007; McLean et al., 2017; Ross et al., 2015; So et al., 2016). It is estimated that 29-38% of the general population display the JTC bias compared to 48-60% of clinical groups with symptoms of psychosis (Dudley et al., 2015). The estimated effect sizes in pooled analysis comparing samples of patients with psychosis with general population samples suggest that patients are likely to have a lower average DTD (g = -0.52 95% CI -0.69, -0.36 Dudley et al., 2015: g -.60, 95% CI -0.77, -0.43; So et al., 2016). However, the heterogeneity of the meta-analyses of the relationship between the JTC bias and psychotic disorders was fairly high (I^2 = 66-77%; Dudley et al., 2015; So et al., 2016).

Meta-analyses have also sought to establish whether the JTC bias is specifically associated with delusions across different mental health contexts. Individuals with delusions across a range of psychiatric conditions have a greater likelihood of reporting the JTC bias (g = 0.76 95% CI 0.44, 1.09) than general population controls (McLean et al., 2017). There is also evidence that individuals with schizophrenia who have delusions are more likely to have the JTC bias compared to those with schizophrenia but no delusions (g=0.33, 95% CI = 0.19, 0.46; McClean et al., 2017). Furthermore, pooled analysis of studies of non-psychotic psychiatric patient samples suggests that there was little difference between performance on the beads tasks compared to general population samples (So et al., 2016), suggesting that the JTC bias is not associated with non-psychotic mental health symptoms.

The heterogeneity of these studies may be due to methodological differences between studies, including the number of trials used in the beads task and the ratio of colours used to increase task difficulty. There is evidence that the use of multiple trials of the beads task is associated with a higher DTD and a lower likelihood of the JTC bias than single trials, and that this contributes to heterogeneity in pooled analysis of the JTC bias for both clinical and general population samples (Dudley et al., 2015; Ross et al., 2015).

In longitudinal studies of clinical samples, it has also been reported that the JTC bias is associated with differences in symptom outcomes. In a sample of patients with first onset of psychosis, the JTC bias was associated with poorer outcomes including greater risk of detainment and a greater number of days hospitalised (median days no JTC group: 15.5, JTC group: 56, Rodriguez et al., 2018; Dudley et al., 2013), which was not explained by IQ or socioecomonic status (Rodriguez et al., 2018). In a study of participants at high risk of psychotic disorder (n=25), a lower DTD was not found to be associated with an increased likelihood of transition to psychotic disorder (transitioned at follow-up: n=5; Winton-Brown et al., 2015). However, the study may not have had the adequate statistical power to detect an effect based on the small sample size.

2.4.2.3 Evidence of the 'Jumping to Conclusions' bias in general population samples

The majority of evidence for the association between the JTC bias and psychosis-related outcomes is from cross-sectional or case-control studies. Evidence of a relationship between the JTC bias and PEs or PLEs has been reported in several studies (Colbert & Peters, 2002; Freeman et al., 2008; Gawęda, Pionke, et al., 2018; Stuke et al., 2017; Tripoli et al., 2020), but not all studies (Ross et al., 2016; So and Kwok, 2015; Ward et al., 2018). Results from a meta-analysis of studies that used the Peters Delusion Inventory (PDI; Peters et al., 2004) to assess delusion-proneness reported a relationship with lower DTD in general population studies ($r = -0.10$ 95% CI = -0.18, -0.02; Ross et al., 2015).

In the largest cohort study of the JTC bias to date (n=4,596; Reininghaus et al., 2018), the JTC bias was examined in relation to both PLEs and affective disturbances: a composite measure of symptoms of depression, anxiety and mania. Participants who reported both affective disturbances and multiple instances of psychosis-like experiences (PLEs) were more likely to display the JTC bias after adjustment for socio-demographic measures, cannabis use, minority status, childhood trauma and working memory (RRR_{adj} 1.57 95% CI 1.19, 2.08). The association was substantially weaker in participants who reported infrequent PLEs and affective disturbances (RRR_{adj} 1.17 95% CI 0.98 – 1.41). As the study only reports sub-group analyses of PLEs according to the frequency in combination with affective disturbance, it is unclear what the strength of the association between the JTC bias and PLEs is without also incorporating co-morbid affective disturbance.

When inducing psychotic symptoms in volunteers by administering methamphetamine or L-dopa, two interventions that are based on the assumption that the JTC bias may be the result of increased dopaminergic activity, there was minimal evidence to suggest that the volunteers were more likely to display the JTC bias compared to controls (Andreou et al., 2014; Ermakova et al., 2014)**.**

2.4.2.3.1 The role of confounding between the JTC bias and psychosis-related outcomes

It is also important to consider whether the relationship between the JTC bias and psychotic outcomes is observable after adjustment for potential confounders. Evidence that the JTC bias is associated with poorer performance on cognitive tasks in both clinical samples (Averbeck et al., 2011; Falcone et al., 2015; Garety et al., 2013; González et al., 2018; Jolley et al., 2014; Ochoa et al., 2014; Rodriguez et al., 2018; Takeda et al., 2018) and general population samples (Ross et al., 2016; Stuke et al., 2017), and that lower cognitive functioning is associated with psychotic symptoms (see review: Reichenberg, 2005) suggests that cognitive functioning is a potential source of confounding in this relationship.

In path analysis of the relationship between the JTC bias and paranoia, there was no evidence of an association after the inclusion of cognitive functioning in the model (Bentall et al., 2009). In a cross-sectional comparison of the JTC bias in groups of participants with (i) psychotic disorder, (ii) PLEs, (iii) relatives with psychotic disorder, and (iv) general population controls, the association between group status and the JTC bias was observable (Van Dael et al., 2006). After adjustment for potential confounders (sex, cannabis use, education level) the relationship between JTC and psychotic outcomes was minimally attenuated (approximately 3%) but was substantially attenuated by additional adjustment for cognitive functioning (approximately 37%; Van Dael et al., 2006). After adjustment for age, sex, ethnicity and IQ in a general population sample (n=1,294), the association between PLEs and lower DTD was attenuated by approximately 55% but remained observable (Tripoli et al., 2020).

The role of current levels of stress during the assessment of the JTC bias may also be a confounding factor, although no studies have adjusted for this. In a general population sample, inducing stress increased the likelihood of both the JTC bias and symptoms of paranoia (Lincoln et al., 2010), although the association between stress and the JTC bias has not been consistently detected in clinical populations (Steffen Moritz et al., 2015; Urbańska et al., 2019).

2.4.2.3.2 Is the relationship between the JTC bias and psychotic symptoms causal?

In a longitudinal study of individuals with symptoms of early psychosis (n=31), a reduction in the likelihood of the JTC bias between baseline and follow-up was associated with a greater likelihood of an improvement in psychotic symptoms (Dudley et al., 2013). However, the relationship between a decreased JTC bias and a greater likelihood of improvement in psychotic symptoms at a year follow-up (n=29) was not found in a similar population (Ormrod et al., 2012). In longitudinal studies of individuals with long-term symptoms of psychosis, the JTC bias was stable when comparing prevalence at baseline and follow-up and there was little evidence of a relationship between the JTC bias and a change in symptoms of psychosis (Peters & Garety, 2006; So et al., 2012).

There is some evidence that interventions that target reasoning processes can decrease the likelihood of the JTC bias and that this is associated with a decline in psychotic symptom severity (Moritz et al., 2011; Moritz et al., 2015; So et al., 2015). However, the association between a post-intervention reduction in the JTC bias and a reduction in psychotic symptoms over time has not been consistently detected (Gawęda et al., 2015; Pos et al., 2018; Ross et al., 2011).

Whilst there is some evidence that targeting the JTC bias in clinical interventions is associated with greater symptom improvement, consistent with a causal relationship between the JTC bias and psychotic symptoms, this relationship may be due to improvement in cognitive ability post-intervention, rather than specifically due to reduction in the JTC bias (Garety et al., 2015). Due to a lack of longitudinal studies that have tested for the association between the JTC bias and the subsequent development of psychotic symptoms, it is not clear whether the relationship between the JTC bias and psychotic symptoms is causal.

2.4.2.3.3 Do risk factors for psychosis increase the likelihood of the JTC bias?

Very few studies have analysed the relationship between risk factors for psychosis and the JTC bias. Traumatic life events were reported to be correlated with a self-report measure of the JTC bias (Gawęda, Pionke, et al., 2018); however, this association was not found by Freeman and colleagues (2008) who also did not find an association between the JTC bias and illicit drug use or loneliness. In an analysis of the EU-GEI study sample (Tripoli et al., 2020), there was a lack of support for an association between increased genetic risk for schizophrenia (indexed by polygenic risk score) and average DTD. In Chapter 6, I further discuss of the limitations of the evidence base for the relationship between exposure to trauma and psychosis-related information-processing biases.

2.4.2.3.4 What cognitive mechanisms account for the 'Jumping to Conclusions' bias?

Investigating the relationship between the JTC bias and other cognitive traits and information processing biases may provide insights into the mechanisms underlying the JTC bias. The JTC bias does not appear to be associated with perceptual traits (impaired verbal self-monitoring or resistance to visual illusions; Bernadyn and Feigenson, 2018; Winton-Brown et al., 2015) associated with psychotic symptoms. There is also a lack of evidence of an association between the JTC bias and attitudes towards decision-making including the ability to re-appraise and revise prior beliefs (belief flexibility) and greater motivation to reach a conclusion (need for closure; McKay et al., 2007; So et al., 2012; Ward et al., 2018).

Several studies have modified the beads task paradigm to include additional self-report measures where participants rate how confident they are about which jar the bead is drawn from. In clinical case-control studies of patients with schizophrenia compared to controls, patients were more likely to report lower confidence in their decisions and were more likely to change their mind about which jar they would selected when given the option (Klein and Pinkham, 2018; McKay et al., 2007; Moritz et al., 2016). These findings suggest that the association between the JTC bias and psychotic symptoms is not due to increased confidence in decisions. Moritz and colleagues (2016) suggest that the JTC bias may be due to a lower threshold of confidence needed before making a decision, referred to as a ‘liberal acceptance’ bias. However, in a small general population sample (n=70) Warman and colleagues (2008) report an association between PLEs and greater confidence in estimations: a trait associated with delusions in multiple task paradigms (for review see Balzan et al. 2015).

Based on current evidence, the JTC bias is due to an abnormality in belief updating. However, results do not suggest that the JTC bias is due to processes such as greater confidence in estimations based on minimal evidence or greater belief inflexibility that define delusional thinking (So et al., 2012; Woodward, Moritz, Menon, & Klinge, 2008). As will be discussed further in the subsequent section, the JTC bias may indicate greater instability in making decisions (based on lower confidence in estimations and an increased willingness to revise estimates rapidly in response to further information). If so, this would suggest that the JTC bias is due to instability in estimating the outcome of an event; a process which may increase the likelihood of prediction errors and affect higher-level information processing. Whether this process is independent of cognitive ability is currently unclear.

2.4.2.4 Probability estimation

While evidence in the previous section exclusively discussed findings from the DTD version of the beads task, there is another version of the task that has been used to gain a greater understanding of belief updating in psychosis. In the probability estimation version of the beads task, which has been used less frequently than the DTD version, participants are presented with a series of beads from one of the two jars. Participants are asked to estimate the probability, on a sliding scale, that the beads have been drawn from one jar or the other after each bead presented in the sequence. Participants are told that the jar that beads are drawn from may change at any time. Therefore, their initial estimates may have to be revised at different stages of the sequence.

There is evidence that participants with psychotic symptoms in clinical and general populations demonstrate an ‘over-adjustment’ bias and revise their beliefs more dramatically when they are presented with information that may contradict their initial estimations (Adams et al., 2018; Colbert and Peters, 2002; Fear and Healy, 1997; Garety et al., 1991; Peters and Garety, 2006; Rodier et al., 2011; Speechley et al., 2010). For example, a participant who has been shown several red beads estimates that there is a high probability the beads are being drawn from the mostly red jar; if, when presented with a blue bead, the participant dramatically revises their estimation to favour the mostly blue jar this indicates an over-adjustment bias.

The extent of over-adjustment bias is more dramatic in those with greater symptom severity: individuals with chronic symptoms of schizophrenia are reported to have higher levels of the over-adjustment bias – revising their probability estimate by up to 100% from one jar to the other when seeing a bead of the opposite colour – compared to individuals with early symptoms of psychosis (Garety et al., 1991; Langdon, Ward, & Coltheart, 2010; Langdon, Still, Connors, Ward, & Catts, 2014). Studies that have taken computational approaches to analyse data from this task to infer what abnormal belief-updating processes contribute to the over-adjustment bias will be discussed in section 2.4.3.

Studies have examined different mechanisms to establish what processes account for the over-adjustment bias. In analyses of the relationship between performance on the 'draws to decision' and probability estimation versions of the beads task, an association between a lower DTD and a greater likelihood of over-adjustment bias has been reported (Langdon et al., 2010; Langdon et al., 2014; Rodier et al., 2011). This finding suggests that there could be a shared mechanism that accounts for the JTC bias and the over-adjustment bias.

The over-adjustment bias is not associated with lower response time or differences in estimations, which suggests that the bias is not due to impulsivity (Peters & Garety, 2006). In a study of the over-adjustment bias in groups with psychotic symptoms, PEs and general population controls, 51% of the sample reported incomprehension of the task, and qualitative analysis established that participants who displayed the over-adjustment bias had thought that beads of different colours had been drawn from separate jars; after providing further instructions on the task and re-testing the participants, the association between delusions and the over-adjustment bias was no longer present (Balzan et al., 2012). However, the introduction of additional information to increase comprehension may have biased participants' responses.

In a pilot study that aimed to minimise incomprehension of the probability estimation task, a sample of students (n=98; Howe et al., 2018) were tested on their comprehension before completing the probability estimation task. Only three participants reported incomprehension and results did not suggest an association between over-adjustment and PLEs. However, differences in samples and psychosis symptoms across studies limit the comparability between the two studies that measure task incomprehension on the probability estimation task.

In studies of participants with psychotic symptoms, it has been observed that the pattern of responses (probability estimates) to consistent information (i.e. series of beads of the same colour) were comparable to control groups but differed when presented with contradictory information; it has argued that this may indicate task comprehension by the participants in the clinical group (Langdon et al., 2014; Peters & Garety, 2006).

A modification of the probability estimation task that aims to gain a better insight into the over-adjustment bias requires participants to make more complicated calculations of probability based on jars with varying ratios of beads (e.g. jar A 80:20, jar B 90:10) and a sliding scale to estimate probability for each separate jar (Speechley et al., 2010). In a study that used this paradigm, people with delusions had a greater likelihood of selecting the jar with the highest proportion of the colour that matched the current bead drawn, interpreted as a bias towards the most ‘hyper-salient’ outcome (the outcome that most strongly matches the hypothesis). Hyper-salience may account for the over-adjustment bias, but the findings have also been interpreted as evidence of task incomprehension (Klein & Pinkham, 2018). These findings highlight the risk of measurement error affecting results from the probability estimation task.

So far, few studies have analysed the role of confounders in the relationship between psychotic symptoms and the over-adjustment bias. In a sub-group analysis of early psychosis patients matched on IQ with general population controls, over-adjustment was associated with symptoms of early psychosis (Langdon et al., 2010), while performance on the task was not associated with IQ in a general population sample (Rodier et al., 2011), indicating that the over-adjustment bias may not be accounted for solely by cognitive functioning. However, further studies are needed to establish the role of confounding in the relationship between the over-adjustment bias and an increased risk of psychotic symptoms.

2.4.2.5 Overview

Studies of the JTC bias have been widely cited as an indication of cognitive processes that contribute to the development and maintenance of delusions and psychotic symptoms. While the relationship between the JTC bias and psychotic symptoms has been replicated in clinical samples, the evidence is less consistent in general population samples. Longitudinally, the

JTC bias and the over-adjustment bias have been shown to be stable over time in longitudinal clinical samples, and there is some evidence to suggest that the JTC bias may be modifiable through cognitive training interventions. However, in both clinical and non-clinical populations, several studies suggest poorer cognitive ability may account for the JTC bias. Poorer cognitive ability may increase the likelihood of task incomprehension and impaired ability to estimate the likelihood of outcomes, which would suggest that the JTC bias is a feature of cognitive impairment rather than an information processing bias independent of cognitive functioning.

In the probability estimation version of the beads task, there is some evidence to suggest that the finding of an over-adjustment bias may be due to task incomprehension. However, this has been challenged by indicators of similar estimations of probability at different points in the task by participants with and without symptoms of early psychosis. If the over-adjustment bias is not due to measurement error, it does suggest that individuals with psychotic symptoms are more likely to dramatically revise estimations in response to contradictory information.

3.4.3 Computational analyses of information-processing biases

Where biological and clinical findings drive the dopamine model, another approach to developing an integrated model of psychosis is based in computational psychiatry, which characterises the brain as a "massive, complex nonlinear computational device that governs the expression of an organism's behaviour" (Anticevic & Murray, 2018). Computational psychiatry aims to successfully model how altered information processing in cognitive and neurological systems, based on computational principals, account for mental disorders. By using computational frameworks to model behaviour based on theoretical principles, mathematical models can be used to test hypotheses formally.

2.4.3.1 The JTC bias: increased cost or decision noise?

In the DTD version of the beads task, participants are not told that there is a fixed penalty to drawing additional beads before making a choice. One hypothesis to account for the JTC bias is that individuals with the bias estimate that there is a higher cost associated with requesting extra beads compared to those who draw more beads. The 'costed Bayesian model' of performance on the DTD task tests this hypothesis by assessing whether a higher subjective value of drawing additional beads is associated with psychotic symptoms. The model also derives an index of the extent to which strategies are inconsistent or due to an unmodelled strategy (decision noise; Moutoussis et al., 2011). In a group of participants with chronic symptoms of schizophrenia, responses on the DTD task were associated with greater decision noise rather than the higher estimated cost of drawing (Moutoussis et al., 2011). This finding suggests that individuals with symptoms of schizophrenia respond more erratically to trials of the DTD task, or that they are employing a sub-optimal strategy of decision making that is not modelled in the study: anything other than 'cost of sampling' is captured by decision noise in this task.

Contrasting findings have been reported in versions of the beads task that have introduced explicit rewards and penalties for behaviour on the task. In a variation of the DTD version of the beads task where participants were presented with feedback as to whether the jar they have chosen is correct, and the cost of drawing a further bead was made explicit (e.g. deduction of 10 points), individuals with symptoms of early psychotic disorder were less likely to adapt to feedback, and a lower DTD was due to a high estimated cost of sampling (Ermakova et al., 2017). The observed differences between these results and those that have used the 'costed Bayesian' model may be due to differences in sample populations or the use of explicit costs for drawing additional beads in this task (Ermakova et al., 2017; Moutoussis et al., 2011).

2.4.3.2 Probability estimation: ‘belief instability’ and ‘circular inference’

In analyses of the probability estimation task (described in section 2.4.2.1), several possible models were tested to account for behaviour on the task, and these provided support for an association between ‘belief instability’ and an increased risk of psychotic symptoms (Adams et al., 2018). Belief instability refers to a bias towards switching estimations between possible outcomes more rapidly and being less able to form stable beliefs based on consistent evidence. As the ‘belief instability’ computational parameter has also been found to successfully model neuronal behaviour in prefrontal cortex networks in cases of schizophrenia (Rolls et al., 2008), Adams and colleagues suggest that belief instability may be a common mechanism to account for differences in both neuronal dynamics and performance on the probability estimation task. In addition to this, decision noise was also associated with psychotic symptoms; consistent with Moutoussis and colleagues’ (2011) finding in the DTD version of the beads task.

Differences in belief-updating have been observed using computational modelling of performance on modified versions of the beads task. In one such version, participants are presented with a single bead and asked to estimate which of two jars with different ratios of coloured beads that bead is drawn from, but with different ratios used in different blocks (e.g. one red bead drawn from: block 1: 90:10 ratio, block 2: 60:40 ratio; Jardri et al., 2017). In a modified DTD task, symptoms of schizophrenia were associated with an abnormal belief-updating style whereby biased prior expectations lead to the misinterpretation of incoming sensory data, which subsequently enforces biased prior expectations in a circular manner (circular inference); this abnormal belief-updating process may contribute to the development of delusions (Jardri et al., 2016, 2017). In another version of the DTD task, where participants are penalised for incorrect guessing or quick decisions, there was an association between giving greater weight to beads drawn earlier in the sequence compared to later-drawn beads and symptoms of early psychosis (Baker, Konova, Daw, & Horga, 2019). Both studies suggest that there is an association between abnormal belief-updating processes the involved sub-optimal weighing of information (circular inference, overweighing early information) and psychosis-related outcomes.

These studies illustrate how hypotheses about the mechanisms (information processing biases) that may contribute to psychosis can be tested using computational models fitted to data from performance on the beads task. As studies have used different versions of the beads task to model different concepts of dysregulated belief-updating (e.g. belief instability, circular inference), replication of these findings is needed using similar computational models in order to establish their implications for understanding psychosis.

2.5 Conclusion

This chapter provides an overview of information processing biases that are associated with psychosis. As illustrated in section 2.2, an association between biased performance on a range of tasks and an increased likelihood of psychotic symptoms have been observed. However, it is unclear whether biases are independent of cognitive functioning and other potentially confounding factors, including increased genetic risk for psychotic disorder and socio-demographic characteristics. An absence of longitudinal studies in general population samples also limits the inferences that can be made about whether abnormal belief updating precedes the development of PEs or changes in symptoms of psychosis over time. There is also a limited number of studies that have tested potential associations between information-processing biases and specific symptoms of psychosis.

Integrated models of psychosis that account for information processing biases suggest that exposure to traumatic stress may increase the likelihood of dopamine dysregulation and consequent information processing biases. Based on the limited empirical research in the area, aberrant salience may be a mechanism that contributes to abnormal belief updating. By incorrectly attributing salience to insignificant stimuli, this may contribute to abnormal belief updating and delusional ideation at higher levels of information processing. This interpretation provides continuity between the dopamine model and the predictive processing model and provides a more comprehensive account by which exposure to trauma can lead to the development of psychosis via biases in information processing. However, as will be discussed in Chapter 6, for many of these information processing biases, robust evidence of association with PEs, or with exposure to childhood trauma, is lacking.

Studies that have used mathematical modelling offer a way to infer what underlying processes account for information processing biases. Studies of psychosis using computational modelling methods are required to provide a clearer picture of how different concepts (e.g. belief instability, circular inference) may inform a unified model of biased belief-updating associated with psychosis.

Chapter 4. Thesis Aims

3.1 Overview

The purpose of this thesis is to carry an in-depth investigation into the relationship between exposure to childhood trauma and psychotic experiences using data from a cohort of young adults based in the UK. As will be discussed, it has been observed that there is an association between exposure to childhood trauma and an increased risk of psychotic experiences (PEs), but there are key gaps in knowledge in this area which the thesis will aim to address. These gaps include whether the observed relationship can be understood to be causal and if the observed increased risk of PEs differs according to the timing, type and frequency of trauma exposure.

Along with investigating aspects of the relationship between childhood trauma and PEs, including the role of timing and confounding, the thesis aims to advance current knowledge about abnormal information processing associated with psychosis and its potential role in the relationship between exposure to trauma and increased risk of PEs. I aim to replicate previously reported observations of associations between abnormal belief-updating processes and PEs using data from a large cohort sample and examine whether these associations are independent of socio-economic background, cognitive functioning and genetic risk for schizophrenia. I will also investigate whether exposure to trauma is associated with an increased likelihood of these information processing biases.

3.2 Childhood trauma and subsequent psychotic experiences

<u>Is childhood trauma associated with subsequent psychotic experiences?</u>

Several studies have reported an association between exposure to trauma and an increased risk of PEs in adulthood (Varese et al., 2012). I will investigate whether exposure to trauma during childhood and adolescence is associated with later psychotic experiences (PEs) at age 18 years. I will assess the extent to which this relationship is likely to be causal by examining the potential roles of attrition bias, measurement error, confounding, and reverse causation in my analyses.

My hypothesis is that there will be an association between exposure to trauma and subsequent PEs that is not adequately explained by alternative (non-causal) explanations.

<u>Does the relationship between childhood trauma and psychotic experiences differ according to trauma timing?</u>

It is not known whether exposure to trauma during different stages of development in childhood and adolescence differ in their association with PEs. Traumatic stress may contribute to lasting biological changes, the extent of which might differ according to the timing of trauma exposure during development. I aim to increase current understanding of the role of timing of trauma exposure on risk of PEs by the comparing effects of trauma during early childhood, mid-childhood and adolescence.

My hypothesis is that there will be an association between exposure to trauma during each developmental period and subsequent PEs however, the effect of trauma on PE risk will be stronger for trauma during early childhood compared to later timepoints.

<u>Does the relationship between childhood trauma and psychotic experiences differ according to trauma type?</u>

Previous studies have observed that there is a difference in the increased risk of PEs according to trauma type, with lower risk for exposure to traumas that involve accidental injury compared to interpersonal violence and with some studies reporting a particularly high risk of PEs following exposure to sexual abuse (Arseneault et al., 2011; McGrath et al., 2017; Moriyama et al., 2018). I will examine different types of interpersonal violence (bullying, emotional neglect, sexual abuse, domestic violence, physical abuse, emotional abuse) to establish whether a specific type may be more strongly associated with an increased risk of

PEs or if different types of interpersonal violence and neglect commonly contribute to an increased risk of PEs.

My hypothesis is that sexual abuse will be more strongly associated with PEs risk compared to other types of interpersonal violence or neglect.

Is there a dose-response relationship between childhood trauma and subsequent PEs?

Previous studies have found a dose-response relationship between exposure to multiple trauma types and further increased risk of PEs and complex mental health outcomes (Crush et al., 2018). I will aim to establish whether reported exposure to several different types of trauma at each of the three developmental stages tested in the study (early childhood, mid-childhood, adolescence) and from age 0-17 years is associated with an increased risk of PEs in a dose-response relationship. In addition to this, the number of developmental stages within which trauma is reported will also be used as an index of chronicity and a measure of dose of exposure.

My hypothesis is that there will be a dose-response relationship between the number of types of trauma exposed to and risk of PEs during each developmental period.

3.3 Belief-updating processes and psychotic experiences

Is there an association between abnormal belief-updating processes and an increased likelihood of psychotic experiences at age 24 years?

As reviewed in Chapter 3, it is unknown whether associations between abnormal belief-updating processes and psychosis in clinical samples is also present for PEs in general population samples and the extent to which these associations are due to confounding. Several studies have analysed the relationship between behavioural indices of abnormal updating processes (e.g. the ‘Jumping to Conclusions’ bias) and psychosis-related outcomes. A smaller number of studies have applied computational models to behavioural data to infer what underlying processes may account for observed biases. I will examine the association between behavioural and computational indices of belief updating processes from performance on probabilistic inferences tasks (two versions of the beads task: draws to decision and probability estimation) and PEs at age 24 years and the extent to which these associations are attenuated by adjustment for confounding.

My hypothesis is that behavioural indices of cognitive biases (JTC, over-adjustment) will be associated with an increased risk of PEs. For computational indices, I do not have an a priori hypothesis around mechanisms of abnormal belief-updating due to the paucity of prior literature in the area.

<u>Is the association between abnormal belief-updating processes and psychotic experiences specific to hallucinations or delusions?</u>

There are some cognitive models of psychosis that propose that there are separate pathways for the development of hallucinations and delusions. To improve understanding as to whether there are separate or shared information-processing mechanisms that contribute to the formation of hallucinations and delusions, I will use bivariate modelling to examine whether associations between abnormal belief-updating processes and hallucinations differ from those for delusions.

I hypothesise that abnormal belief-updating processes will be more strongly associated with delusional beliefs than hallucinations.

<u>Is there an association between abnormal belief-updating processes and an increased likelihood of depression or anxiety?</u>

In addition to PE symptom specificity, it is also not known whether abnormalities in performance on information processing tasks are specifically associated with PEs or if these performance indices are also associated with anxiety and depression that commonly co-occur with PEs. I will use multivariate probit modelling to compare the strength of association between the cognitive bias indices and each of the three outcomes.

I hypothesise that there will be a specific association between abnormal belief-updating and PEs and that there will be little association between abnormal belief-updating and depression or anxiety.

3.4 Childhood trauma and abnormal belief-updating processes

Is there an association between exposure to trauma and an increased likelihood of information-processing biases associated with psychosis?

Theoretical models of the causal pathway of psychosis suggest that trauma could lead to information-processing biases that contribute to the development and maintenance of delusions and hallucinations. I will investigate the extent to which previous studies have investigated this relationship by carrying out a systematic review and meta-analysis of studies that have investigated the relationship between exposure to childhood trauma and information processing biases to identify gaps in the literature and inform the empirical analyses in my thesis.

Is there an association between exposure to trauma and an increased likelihood of abnormal belief-updating processes?

Using behavioural and computational indices of abnormal belief-updating processes from the probabilistic inference tasks, I will test whether there is a relationship between exposure to trauma and an increased likelihood of abnormal belief-updating processes. I will use results from the analysis of abnormal belief-updating processes and PEs to identify any abnormal belief-updating processes that are associated with both exposure to trauma and PEs that may be candidate mediators on this pathway.

I hypothesise that trauma will be associated with behavioural indices (the JTC bias, overadjustment bias) and computational indices that are also associated with PEs.

3.5 Childhood trauma, abnormal belief-updating processes and psychotic experiences

Do abnormal belief-updating processes mediate the relationship between exposure to childhood trauma and an increased risk of subsequent psychotic experiences?

As discussed in Chapter 2, theoretical models suggest that information-processing biases are potential mediators on the causal pathway from trauma to PEs. Using the most appropriate measures based on the results from the aims above, I will conclude the thesis by investigating the potential mediating role of cognitive bias indices on the pathway from childhood and adolescent trauma to PEs in early adulthood.

I hypothesise that indices of abnormal belief-updating will partially mediate the association between trauma and a greater likelihood of PEs.

Chapter 5. Study Sample and Methodology

5.1 Overview

Studies I and III use observational data provided by participants of the Avon Longitudinal Study of Parents and Children (ALSPAC). This chapter will give an overview of the methods used for studies I and III. The first section of the chapter is an outline of study designs that use observational data and the strength of causal inference that can be made from these designs. The subsequent sections provide a brief description of the study sample, measures and the statistical methodology used for studies I and III.

5.2 Observational study methods and causal inference

There are a range of study designs that can be used to collect, analyse and establish the relationship between an exposure and outcome using data collected from sample populations. Observational studies are used either to develop models for the prediction of an outcome (where causality is not a requirement) or to identify causal effects, as is the focus of this section.

A key consideration for these various study designs is the strength of evidence they can provide in support of a causal relationship between the exposure and outcome. The strength of this evidence is based on how well a study design minimises the possibility that the observed results are not due to non-causal factors.

4.2.1 Non-causal explanations of observed association in observational studies

<u>Chance</u>

Evidence of an association may be due to random error or sample variation. A p-value, which is the probability of detecting the same observed difference between groups, or one larger than that observed, if the null hypothesis is true, is an index of the likelihood that observed results are due to chance. It has been common practice for a p-value of less than 0.05 to be considered ‘statistically significant’ and evidence to support a hypothesis. However, this interpretation of the p-value has been widely criticised because of the use of an arbitrary threshold of significance, and researchers are encouraged to present and interpret p-values as the strength of the evidence against the null hypothesis within the context of the results (‘It’s time to talk about ditching statistical significance', 2019; Sterne & Davey Smith, 2001; Wasserstein, Schirm, & Lazar, 2019).

Reverse causality

Reverse causality refers to how an outcome may cause the exposure as opposed to the hypothesised direction of causality between an exposure and outcome. It is particularly difficult to exclude the potential influence of reverse causality from studies where the exposure and outcome are assessed at the same time.

Bias

There are several sources of systematic error that can bias results. Different types of biases are broadly categorised as errors concerning participants included in a study (selection bias) and errors in the information collected from the participants (information bias). Features of the study design or analysis that have created systematic errors can lead to either over or under-estimates of the true exposure-outcome associations.

Confounding

Confounding means that an observed association can be partially or completely accounted for by a variable that is associated with the exposure and causally related to the outcome but is not on the causal pathway between them. Confounding can also mask causal associations. The influence of confounding can be minimised during the design stage of a study (e.g. matching or randomisation of participants) and the analysis stage (e.g. stratification or multivariable regression modelling).

4.2.2 Explanations for lack of observed association in observational studies

Explanations for failing to observe evidence of a causal association include confounding, bias, and inadequate statistical power (Type II error) for the study to detect an effect of that magnitude.

4.2.3 Study Designs

<u>4.2.3.1 Randomised Control trials</u>

Randomised control trials (RCTs) are considered ‘gold standard’ study designs for assessing causal relationships. RCTs randomise participants to different exposure conditions and then assess them at a later time-point to compare the incidence of the outcome between the groups. Evidence from these trials can provide the strongest evidence of causality as the design has the potential to minimise the risk of observed associations arising from non-causal factors, and most particularly from confounding and selection bias. However, there are several situations where the use of an RCT study design is not appropriate, ethical or pragmatic to address a research question, and in such situations, evidence of causality is limited to observational study designs.

<u>4.2.3.2 Observational Study Designs</u>

In cases where trials are unsuitable or unfeasible to carry out, the relationship between the exposure and the outcome can be established by analysing information from participants who vary naturally in their exposure status. As the exposure in these designs is not randomly allocated, there is a higher risk of detecting non-causal sources of association. These study designs include the following:

Cohort studies

A cohort study is a longitudinal study design that samples people based on their exposure status (e.g. born in a particular area, of a certain age, have been exposed to an environmental risk factor) and in which participants are followed up to identify new-onset outcomes. These studies are less prone to reverse causation all selection bia 4.4.1.1s than other observational designs.

Case-control Studies

In a case-control study, participants are sampled and grouped according to whether they do (case group) or do not have (control group) a particular outcome (e.g. disease diagnosis). The case and control groups are compared to establish if exposures hypothesised to contribute to the outcome differ between the groups. This study design is particularly likely to be affected by selection bias, reverse causation and recall bias because the exposure and outcome are assessed at a single point in time.

Cross-sectional studies

A cross-sectional study surveys a population to measure the relationship between an exposure and outcome at a specific time point in time and is also likely to be affected by selection bias, reverse causation and recall bias.

4.3 Study sample: Avon Longitudinal Study of Parents and Children

The ALSPAC cohort was established as part of the European Longitudinal Study of Pregnancy and Childhood (ELSPAC), a series of longitudinal studies in defined geographical areas in Europe designed to determine genotype and environmental factors that contribute to health outcomes for parents and children during development. The ALSPAC cohort recruited pregnant women resident in areas of South West of England with an expected date of delivery between 1st April 1991 and 31st December 1992, which led to the enrolment of 14,541 women (Boyd et al., 2013). Later phases of recruitment that sampled from the same eligibility criteria as original participants took place when the cohort children were approximately aged 7 years onwards and led to an overall total of 15,247 enrolled women (Boyd et al., 2013).

4.3.1 Enrolment

Eligible pregnant women were recruited from September 1990 through a variety of methods. Local advertising was used in the area, ALSPAC staff approached mothers when attending routine ultrasound test, and medical personnel including community midwives were asked to discuss the study with eligible participants (Golding et al., 2001). Once participants expressed an interest in the study, ALSPAC team members contacted eligible participants and discussed the confidentiality of the study, its benefits and their right to discontinue their involvement in the study.

4.3.2 Ethical Approval

Ethical approval for the ALSPAC study was initially provided by local health authorities (Bristol and Weston, Southmead and Frenchay). Details of ethical approval can be found at http://www.bristol.ac.uk/alspac/researchers/research-ethics. The study benefitted from the establishment of its own ethics and law committee, which approves all self-completed questionnaires.

4.3.3 Data Collection

Data from these participants have been collected through questionnaires, clinic sessions, collection of biological samples and record linkage with the Office of National Statistics registries. Based on the most recent cohort profile, between birth and approximately 18 years of age, there have been 68 data collection timepoints, which has included the collection of 34 child-completed questionnaires, 9 clinical assessment and 25 questionnaires completed by caregivers (Boyd et al., 2013).

4.3.4 Representativeness of cohort

As discussed by Boyd and colleagues, the geographical focus of ALSPAC recruitment to a small area in the UK assisted the establishment and identity of the cohort but also restricted the generalisability of the cohort to the national population (Boyd et al., 2013).

As ALSPAC did not recruit all eligible mothers to the study, systematic differences between those who were and were not recruited in the Avon area may have been introduced from the initial recruitment onwards. When comparing the demographic characteristics between ALSPAC cohort participants who completed a postnatal questionnaire eight months into the study with 1991 census reports in Avon, ALSPAC participants were more likely to report owning a house and being married and less likely to be of non-white ethnicity (Golding et al., 2001). As 80% of enrolled participants completed the questionnaire at eight months, this observation reflects both the incomplete enrolment of all eligible participants in the Avon area and non-response from participants to this questionnaire.

Over the course of the ALSPAC study, demographic differences between attendees compared to both ALSPAC non-attendees and the national population have been observed. In the assessment of mothers at the ALSPAC clinic between 17-18 years after pregnancy, participants who did not attend this clinic were more likely to not have a university degree at the time of pregnancy and have a head of household in a manual occupational social class

(Golding et al., 2001). Children enrolled in ALSPAC are reported to have higher academic attainment at age 16 years compared to nation-wide assessment data (Boyd et al., 2013).

4.3.5 Samples used in the thesis

As will be outlined in results chapters for the respective studies, the samples used from the ALSPAC cohort differed according to the number of participants who completed the assessment of the outcomes of interest. For study I, only participants who attended assessment of PEs at age 18 years were included. Samples for Study III were drawn from those who completed assessments at age 24 years of cognitive and perceptual biases, depression, anxiety and PEs. Flow charts to illustrate these samples are included in 0 for study I and Chapter 7 for study III.

4.4 Measures

4.4.1 Study I & III exposure variable: childhood trauma

Based on literature relating to psychotic symptoms (see Chapter 1), measures of childhood trauma that were analysed in studies I and III were exposures to trauma that involved interpersonal victimisation, sexual abuse or neglect. Questions relating to these exposures were answered by participants of ALSPAC during different age-periods throughout the study, along with questions relating to adversity and less severe instances of stress. In some cases, questions relating to stressful exposures had multiple response options that ranged in severity from mild to severe. To have suitable measures of exposure to trauma, I derived binary measures of exposure to different types of trauma by selecting appropriate questions from variables collected in ALSPAC.

4.4.1.1 Development of selection criteria

In order to have measures of trauma that reflected experiences that would be highly upsetting to anyone who experienced them, I carefully assessed the content of questions and appropriate response options for all trauma-relevant questions collected during the ALSPAC study. Questions related to child adversity from the ALSPAC cohort were identified by Dr Lotte Houtepen (2018) and I examined these to identify which measures were relevant to my study.

Questions were selected based on the following criteria:

i) how clearly the question refers to a type of trauma exposure identified for inclusion
ii) The question has a response option that refers to chronic or severe stressors that would be considered traumatic

Figure 4.1 is a flow chart of selection of questions from ALSPAC. Figure 4.2 provides definitions of each type of trauma included in the measure and examples of questions and their response options (e.g. the most severe response options from questions with categorical response options) that were included in measures of trauma. A full list of questions included in the measures of trauma and which categorical responses to trauma were included to derive binary options of trauma are listed in Appendix Table 2.1.

Figure 4.1 Flow chart of the process of selection of variables for trauma measures

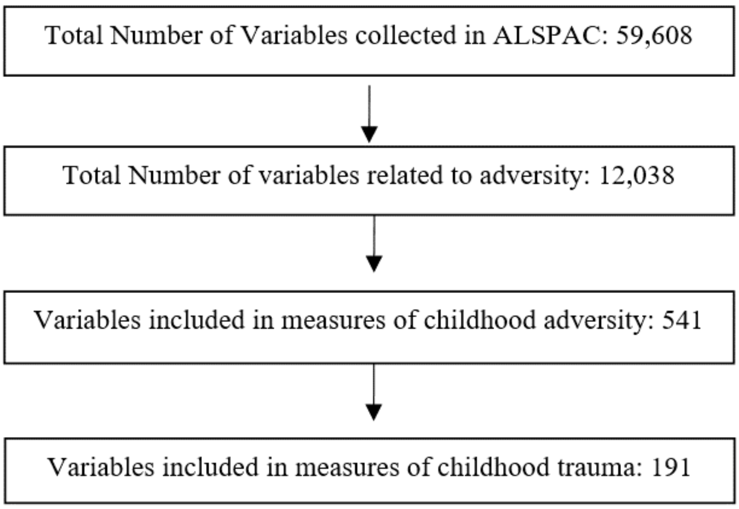


Figure 5.2 Trauma types included in trauma exposure measure and example binary derivation of questions from ALSPAC questionnaires

Type	Definition	Question and Classification Example
Domestic Violence	Parents violent towards each other, including hitting, choking, strangling, beating	'Has your partner has ever threatened you with a knife or other weapon?'
Bullying	Report frequent bullying or specifically threatened/blackmailed (ranging 4+ in last 6 months to weekly)	'How often have you been threatened or blackmailed?' (more than four times in the last six months classified as bullying)
Sexual Abuse	Ever sexually abused, forced to perform sexual acts or touch someone in a sexual way	'Has an adult or older child forced, or attempted to force, you into sexual activity?
Emotional Neglect	Child always felt excluded, misunderstood or never important to family, parents never asked or never listened when child talked about their free time	'How often does a caregiver know where you were going, when you went out, in the last year?' ('never' classified as emotional neglect);
Emotional Abuse	Parent was ever emotional cruel towards child or often said hurtful/insulting things to the child	How often has an adult in the family said hurtful or insulting things to you?' ('often' or 'very often' classified as emotional abuse);
Physical Abuse	Adult in family was ever physically cruel towards or hurt the child	'In the last year, has someone hit, kicked, punched or attacked you with the intention of really hurting you?'

Note: Questions with categorical response options that are then classified into a binary measure of trauma are specified in parentheses

4.4.1.2 Types of trauma measured

Measures of different types of trauma were derived based on previous literature, discussion with supervisors, and reviewing available data as follows:

Physical abuse

Questions relating to physical harm to the participant from caregivers and other adults from questionnaires completed by caregivers.

Emotional Abuse

Participants were asked whether adults had said hurtful or insulting things to them or if they were threatened with physical harm: responses of ‘often’ and ‘very often’ were recorded as an indicator of emotional abuse. Parents were asked whether their children had been exposed to emotional cruelty by themselves or their partners.

Emotional Neglect

These questions were based on self-report questions relating to how often caregivers take an interest in aspects of the participants’ lives, including their whereabouts and what they do in their spare time. Participants who responded ‘never’ to these questions were identified as being emotionally neglected.

Bullying

Questions relating to victimisation included a wide range of forms of bullying (i.e. name-calling, blackmail, assault). I selected questions that referred to instances of bullying that would be the most likely to be highly distressing and traumatic: this included any form of physical assault and threats of assault or blackmail.

Sexual abuse

Caregivers’ reports of whether their child had been exposed to sexual abuse were recorded as indicators of sexual abuse in early life. Any positive response from participants to questions that refer to any adult or older child forcing or attempting to force them into sexual activity was recorded as exposure to sexual abuse. Whilst participants were asked on a number of occasions throughout adolescence about ‘being made to engage’ in sexual acts with a romantic partner, the pattern of responses suggests that participants did not interpret these questions as referring to sexual assault, probably as the main focus of the questionnaire was on consensual sexual activity. I, therefore, did not include information from these questions in my measure of sexual abuse.

<u>Timing of trauma</u>

Once questions were selected, I divided them according to the age-period that the questions referred to (for a summary see Figure 5.). The three age-periods that trauma was measured were early childhood (0-4.9 years of age), mid-childhood (5-10.9 years of age) and adolescence (11-17 years of age). Data relating to these age-periods were collected primarily during these age-periods. As there were no self-report measures of sexual abuse during childhood or adolescence and other trauma exposures during childhood and these were likely to be underreported by parental report, I supplemented measures with data from a questionnaire at age 22 years that referred to events occurring before 10.9 years of age (mid-childhood) or between ages 11 and 17 (adolescence).

<u>Measures of trauma dose</u>

I also derived measures of trauma that reflected increasing levels of exposure to ascertain whether there is a dose-response relationship between exposure to trauma and the risk of the outcomes in study I and III.

I derived two measures of frequency: (i) the number of different types of trauma reported by a participant, and (ii) the number of age-periods that participants reported exposure to trauma. As there were few participants who reported exposure to more than three types of trauma, I grouped these into a single category in the frequency measure (3+ exposures).

Figure 5.3 Measures of trauma according to age-period

Age-periods	Binary Measures (Y/N)	Categorical measures
Age 0 – 4.9 years	Physical abuse, sexual abuse, emotional abuse, bullying, exposure to domestic violence	Number of trauma types reported (0, 1, 2, 3+)
Age 5- 10.9 years	Physical abuse, sexual abuse, emotional abuse, bullying, exposure to domestic violence, emotional neglect	Number of trauma types reported (0, 1, 2, 3+)
Age 11-17 years	Physical abuse, sexual abuse, emotional abuse, bullying, exposure to domestic violence, emotional neglect	Number of trauma types reported (0, 1, 2, 3+)
Age 0-17 years	Physical abuse, sexual abuse, emotional abuse, bullying, exposure to domestic violence, emotional neglect	Number of trauma types reported (0, 1, 2, 3+) Number of age-periods with any trauma type reported (0, 1, 2, 3)

4.4.1.3 Minimum response criteria for complete-case data

Questions for each category of trauma were selected from a wide range of questionnaires, and missing data varied for each questionnaire. I wanted to avoid classifying an individual as not exposed to trauma if they had participated in very few assessments from age 0-17 years. To address this, I established a minimum threshold of completion of at least 50% of the questionnaires that contributed to a particular derived measure of trauma before a participant was classified as non-exposed for that measure; individuals with less than 50% completion and only negative responses on these were classified as having missing data. Individuals who reported trauma in any assessment were classed as exposed regardless of missing data.
A detailed description of this coding procedure is included in Appendix Table 2.2.

4.4.2 Studies I & III outcome measure: psychotic experiences

Measurements of PEs were collected during clinic visits at approximately ages 12, 18 and 24 years using the PLIKSi semi-structured interview (Horwood et al., 2008; Zammit et al., 2013). Details of the specific measures used from the PLIKSi data at each period for different studies are described in the methods sections for study I (0) and study III (Chapter 7).

The PLIKSi interview consists of questions that allow for rating of 12 core psychotic experiences covering: delusions (spied on, persecution, thoughts read, reference, control, grandiosity, unspecified), auditory or visual hallucinations, and experiences of thought interference, including broadcasting, insertion, and withdrawal. After asking an initial structured stem question, interviewers were free to probe participants using a cross-questioning approach to determine if any self-reported reported experiences met criteria for a psychotic experience. The rating rules and glossary for these items were based on Schedule for Clinical Assessment in Neuropsychiatry (SCAN; Aboraya et al., 1998) definitions.

Interviewers also asked about frequency of experiences, impact on social functioning, help-seeking from professionals, age of onset of experiences, and whether experiences were wholly attributed to sleep or fever. Based on these responses, the interviewer could rate experiences as being not present, suspected or as definitely psychotic experiences. In cases where assessors were uncertain of which coding category to use, symptoms were 'rated down' to avoid false positives (Zammit et al., 2008, 2013).

4.4.3 Study III measure: belief-updating tasks

Cognitive and perceptual biases were assessed using three tasks that were completed by ALSPAC participants during clinical assessments at approximately 24 years of age. Measures were derived using different methods for each task paradigm. Derivation of measures was carried out by researchers in cognitive neuroscience and computational psychiatry, and the use of these variables in study III will be described in Chapter 7. To increase the likelihood of task comprehension, participants completed a trial run of each task and assessors asked participants if they understood the tasks.

Figure 5.4 List of confounders used in the thesis

Category	Variable	Variable type	Measure
Socioeconomic status	Maternal education	Categorical	Mother's GCSE attainment (<O-level, O-level or >O-level)
	Crowded living conditions	Categorical	Number of children per bedroom
	Social class	Categorical	Occupational class
	Income	Categorical	Equivalised income reported between 33-47 months of age separated into quintiles
Measures of family adversity	Parental drug use	Binary	Parental self-report measure when child was less than six months old
	Parental mental health problem	Binary	Parental self-report measure when child was less than six months old
	Parent-reported criminal activity	Binary	Parental self-report measure when child was less than six months old
Cognitive performance	IQ at 8 years old	Continuous	Wechsler Intelligence Scale for Children (WISC) measured at 8 years old
	Executive Function	Continuous	Normative score on opposite worlds task from Test of Everyday Attention for Childhood (TEA-Ch) at 8 years old (Manly et al., 2001)
	Working memory	Continuous	WISC-III Digit Span task (Martin et al., 2015)
Genetic Risk of psychopathology	Mother's risk of schizophrenia	Continuous	Polygenic risk score (PRS; derived by Jones and colleagues (2016)
	Risk of schizophrenia	Continuous	PRS
	Risk of major depressive disorder	Continuous	PRS
	Risk of bipolar disorder	Continuous	PRS
	Risk of neuroticism	Continuous	PRS
Developmental measures	Childhood temperament	Continuous	Carey Infant and Toddler Temperament Scales (Sayal et al., 2014) at 6 months old
	Developmental delay	Continuous	Denver Developmental Screening Test (Iles-Caven et al., 2016) at 18 months

4.4.3.1 Inclusion of confounders in analytic models

In study I, I examined socioeconomic status, indicators of family adversity, developmental variables and genetic risk of psychopathology (listed in Figure 4.3) as potential confounders in the relationship between trauma and PEs. As inclusion of all potential confounders resulted in a substantial reduction in sample size due to missingness, and as I was yet to develop the first imputation model of the thesis, I decided that the most feasible approach was to use a data-driven approach to select which confounders to include in the main analysis model (Kirkwood & Sterne, 2003). I examined the change in the exposure-outcome estimates after individually adjusting for each potential confounder, and then in the main analysis model adjusted only for those variables that changed these estimates by 5% or more.

In study III, I identified cognitive performance, socio-economic status and genetic risk of psychopathology as potential sources of confounding and included these in my analytic models.

4.5 Statistical Methods

This section will give a brief outline of the statistical methods used in the thesis and the tests of assumptions underlying the statistical methods used. Descriptions of the specific methods for each study are stated in later chapters of the thesis: study I (0), study III (Chapter 7).

4.5.1 Regression Analyses

Measures of psychopathology outcomes (PEs, symptoms of hallucinations and delusions, anxiety and depression) were all binary outcomes, and logistic regression was used as the main analysis model. Measures of indices for the information processing task, that are analysed as outcomes in analyses with exposure to trauma, are categorical, binary and continuous.

For the analysis of exposure to trauma and belief-updating processes, I examined as outcomes a range of continuous, categorical and dichotomous measures of performance on the cognitive and perceptual bias tasks described in Chapter 7. I used linear regression (for continuous, normally distributed outcomes), logistic regression (binary outcomes) and multinomial regression (categorical outcomes) as appropriate. Outcomes using multinomial and logistic regression are reported as odds ratios and outcomes using regression analyses as regression coefficients (β). The 95% confidence intervals and p-values are also reported.

4.5.2 Multivariate probit analysis

For analysis of information-processing biases, I modelled the outcomes of (i) hallucinations and delusions and (ii) depression, anxiety and PEs in bivariate and multivariate probit models respectively. While link functions differ between analyses, the results from both methods are very similar, and probit estimates can be interpreted as odds ratios by multiplying estimates by 1.6 (Stern, 1989). The conventions of using logit and probit regression differ between disciplines: logit functions are more widely used in epidemiology, whereas probit is favoured in econometrics. The difference between probit and logit models where there are multiple outcomes is that probit modelling assume that outcomes are correlated, whereas logit models do not. I felt that the assumption that the mental health outcomes that model as multiple outcomes in single models (hallucinations and delusions; PEs, depression and anxiety) are likely to be correlated is plausible and that, therefore, bivariate and multivariate probit modelling were suitable for these analyses.

In the bivariate probit modelling of hallucinations and delusions, I used wald tests after imputation to test if there was a difference between the estimated effects between each information processing parameter and hallucinations and delusions. For multivariable probit estimations, I used the MLwiN package to test associations in imputed data and reported probit estimates converted into odds ratios as effect estimates.

4.5.2.1 Testing assumptions of linearity (dose-response effect) of categorical exposures

I used likelihood-ratio tests to determine whether the relationship between a categorical exposure and an outcome was linear by comparing two regression models using likelihood ratio testing. The likelihood-ratio test tests the null hypothesis that there is no difference between models that treat the exposure either as a linear variable or as a categorical variable by using dummy/indicator variables. A non-significant likelihood ratio statistic (LRS) suggests that the exposure categories can be assumed to have a linear (incremental) effect on the outcome, and the effect size interpreted as a change in outcome per unit increase in exposure.

4.5.2.2. Mediation analysis

I used mediation analysis to examine the extent to which abnormal belief-updating processes mediated the relationship between exposure to childhood trauma and an increased likelihood of PEs. I estimated the total estimated effect and indirect effect using logistic regression using the ‘paramed’ command in STATA using imputed data, and estimations were combined using Rubin’s rules. The paramed function uses parametric regression models and extends the earlier regression-based approach, referred to as the Baron and Kenney method (Baron & Kenny, 1986), by also allowing for interactions between exposure and mediator interactions in the regression model. I selected abnormal belief-updating indices as candidate mediators only where there was evidence from regression analyses of their association with both PEs and exposure to trauma.

4.5.3 Missing data

For studies I and III, the proportion of missing data for the exposure variables for those in the study sample meant that bias from attrition might be introduced into the analyses. At later times of assessment during ALSPAC, the rates of missing data are greater as more participants discontinue involvement, and this bias may be further pronounced. This is relevant to both studies using data from the ALSPAC cohort in the thesis as outcomes are from data collected at age 18 years and age 24 years.

4.5.3.1 Missing data assumptions

Missing data is understood to be caused by different mechanisms: Missing at random (MAR), missing completely at random (MCAR) and missing not at random (MNAR). These mechanisms are important to consider as they each have different implications for the sources of bias that may affect results from analyses and the statistical approaches that may be appropriate for approaching them (Miquel Porta (ed.), 2014; Sterne et al., 2009). The patterns of missingness are defined as the following:

MCAR: There are no systematic differences between responders and non-responders; therefore, a random sample of data is missing (i.e. there is no relationship between the missingness of the data and any values that are observed or missing).
MAR: There is a systematic relationship between the propensity of missing values and the observed data, but not the missing data. Systematic differences between the observed and missing data can be accounted for by observed data.
MNAR: There is a relationship between the propensity of the value to be missing and its values. Systematic differences remain after taking into account the observed data.

Missing data that is likely to be MNAR can introduce bias into results. For example, if individuals who are prone to paranoia are less likely to attend an assessment of psychosis, this may bias a study of PEs. If missing data can be assumed to be MAR, statistical approaches can be used to use information from partially observed variables to reduce bias and carry out analysis that has more statistical power than complete-case data. There is no statistical method to test whether data are MAR or MNAR, but steps can be taken in handling missing data to make the MAR assumption more plausible and hence to minimise potential bias.

4.5.3.1 Methods of handling missing data

There are ad hoc approaches to addressing missing data, which include deleting cases or variables to reduce the amount of missing data or replacing values with observed values (e.g. mean value or last measured value). These approaches are likely to introduce bias into estimates. A more rigorous approach to handling missing data is the use of multiple imputation.

4.5.3.2 Multiple imputation

Imputation is a method that replaces missing values with a value that could have plausibly been reported. The process involves creating a dataset that has values for missing data that are based on the distribution of observed data and covariates specified in the imputation model. The aim of this process is not to fill the missing field with the value that is most likely to have been completed by a specific participant but to fill missing fields with values that maintain the integral characteristics of the dataset. With a single imputation the values imputed are appropriate, but the variance is under-estimated and does not reflect the variance of a real data sample.

To address the limitations of a single imputed dataset, multiple imputation creates multiple datasets that simulate the variance from multiple random draws from a sample population. The combined values of these multiple datasets are then used in the analysis to give an overall estimation of the association. This means that the imputed values are close to the true population value for both mean and variance and minimise the bias introduced by missingness. This method can be used in cases where data may be MNAR as the use of covariates that may contribute to missing data can make the MAR assumption more plausible. To use imputed models to fit regression models, estimated effect size values from each imputed dataset are averaged to give a single overall effect estimation based on Rubin’s rules (Sterne et al., 2009). This method is widely used and considered a reliable way to address potential bias from missing data.

4.5.3.3 Using multiple imputation in Studies I and III

As observed by several studies that have used data from ALSPAC (Howe et al., 2013), recruited participants who stop completing assessments at later timepoints are more likely to be from a lower socioeconomic background and have lower educational attainment compared to those who remain in the cohort. These findings inform the assumption that missing data in the cohort are MAR when including covariates related to the lower socio-economic position in the imputation model.

To carry out the imputation, I used the ‘ice’ command in STATA version 15. This uses the ‘MICE’ system of chained equations to perform the multiple imputation (Royston, 2004). A chained equations model generates the imputed dataset first by using random sampling to fill in missing data and then replacing these values with the value generated from the specified regression equation for the incomplete variable. This, in turn, takes place for each incomplete variable in the dataset and the complete process is a single imputation ‘cycle’ (Azur et al., 2011). This cycle is repeated multiple times to produce a single imputed dataset, which ensures that the values are stable and more likely to converge to produce imputed values plausible for the dataset. This process is then repeated to produce a specified number of multiple imputed datasets. A chained equation model is more flexible than other imputation methods as it allows binary, continuous and categorical variables to be imputed in a single model because each incomplete variable has its specified regression equation. I used predictive mean matching for non-normally distributed continuous variables in my imputation models; a technique which specifies that the imputed values of a variable closely match the distribution of the observed data.

The analysis strategy used for imputed data models was largely identical to the complete-case analysis, which I completed for each analysis model to compare effect sizes. I specified that the analysis used was for imputed data by using the ‘mi estimate’ command.

4.5.3.3.1 Selecting covariates for the imputation model

As stated by Sterne and colleagues (2009), the MAR assumption for incomplete data is made based on the suitability of selected covariates to account for missing data. Selecting covariates that are likely to account for missing data in the imputation model is integral to minimising bias in the analysis. It is recommended that all variables in the main analysis are included in each imputation equation and that a wide range of variables that are either: (i) likely to predict the missing value themselves, (ii) related to what is likely to be causing missing data.

I followed these criteria for the selection of covariates in each of the imputation models and included all main analysis variables in each imputation equation. I used measures of socio-economic status and markers of adversity to predict values for all incomplete trauma data in both models. Exposure to trauma at early timepoints, where there was a lower proportion of missing data compared to later measures, was used to predict exposure to trauma at later timepoints.

4.5.3.3.2 Including interaction terms in the imputed data analysis

In sensitivity analysis for study I, I repeated the main analyses omitting participants who report suspected or definite PEs at age 12 years to test potential reverse causal effects from participants who were assessed as having PEs before trauma exposure; this required predicting missing values for PEs at age 12 years. In the imputation model for this analysis, it is important to consider that there may be an interaction between PEs at age 12 years and reported PEs at age 18 years. As described by Tilling and colleagues (2016), not including interactions in an imputation model can give rise to biased estimates. To address this, I included an interaction term for PEs at age 12 years and PEs at age 18 years in the imputation model used for this analysis.

Chapter 5 Study I: The Relationship Between Childhood Trauma and Psychotic Experiences at Age 18 Years

5.1 Background

As discussed in Chapter 2, there is evidence that people exposed to trauma have a higher risk of psychosis- related outcomes. Meta-analyses show that individuals exposed to trauma have a 2-3 fold increase in the risk of psychotic symptoms (Cunningham et al., 2016; Trotta et al., 2015; Varese et al., 2012). Previous cohort, case-control and cross-sectional studies have observed this relationship. As previously discussed, methodological issues and the heterogeneity of the evidence base limits interpretation as to whether the relationship is causal and to what extent non-causal factors (confounding, bias, reverse causation) contribute to the observed associations.

The effect of trauma on the risk of PEs may be affected by the timing of the trauma during development and the type of trauma exposure. Few studies have analysed trauma exposure at multiple time-periods and according to several trauma-types, which limits the current evidence base. Alternatively, the effect of exposure to repeated trauma may have a greater effect on PEs risk than exposure to a specific type of trauma or during a particular developmental period. Gaining a greater understanding of these differences may be able to inform current models of psychosis pathways and possibly help identify people at elevated risk of PEs. Therefore, further investigation is needed to address these gaps in the current evidence base.

There is some evidence that the relationship between trauma and psychotic symptoms differs according to the type of trauma exposure experienced. Interpersonal violence and neglect are associated with an increased risk of psychotic symptoms to a greater extent compared to accidental harm, financial disadvantage or parental loss (Arseneault et al., 2011; McGrath et al., 2017; Spauwen et al., 2006). For different types of interpersonal violence and neglect, it is less clear whether these trauma types are differentially associated with the risk of PEs. There is some evidence that sexual abuse is more strongly associated with psychosis risk than other types of trauma (Bebbington et al., 2004; De Loore et al., 2007; Lataster et al., 2006; McGrath et al., 2017; Nierop et al., 2014). However, confidence intervals for the estimated effect of sexual trauma on PEs often overlap with those for other types of trauma exposure (McGrath et al., 2017; van Nierop et al., 2014).

Few studies have examined whether there are periods of vulnerability during childhood and adolescence and these have not reported consistent timing-specific effects of exposure to trauma on the risk of PEs (Arseneault et al., 2011; Spauwen et al., 2006; Wigman et al., 2011, detailed in Section 1.4.1.4).

Several cross-sectional and cohort studies have also observed that there is a dose-response relationship between the number of types of trauma reported and an increased risk of PEs (Arseneault et al., 2011; Bentall et al., 2012; De Loore et al., 2007; McGrath et al., 2017; Moriyama et al., 2018; Shevlin et al., 2008). Establishing that there is a dose-response increase and that this relationship is observed across multiple age-periods and is robust to confounding, would support the hypothesis that the relationship between exposure to trauma and risk of PEs is causal.

Establishing whether observational evidence supports the thesis that the relationship between exposure to trauma and PEs is causal, and the size of this effect, is integral to providing the basis for studies of potential mechanisms on this pathway (Williams et al., 2018) and that can inform models of psychosis and potential intervention strategies.

5.2 Aims of the chapter

This chapter aims to address the following questions:

1. Is exposure to trauma involving interpersonal violence and emotional neglect associated with an increased risk of PEs?
2. Does this relationship differ according to the timing of traumatic exposure (early childhood, mid-childhood, adolescence)?
3. Does this relationship differ according to the type of traumatic exposure (bullying, emotional neglect, sexual abuse, physical abuse, emotional abuse, witnessing domestic violence)?
4. Does the risk of PEs increase according to the dose or frequency of trauma experienced (based on exposure to either how many different types of trauma, or the number of age-

periods (early childhood, mid-childhood, adolescence) between ages 0-17 that these occurred)?

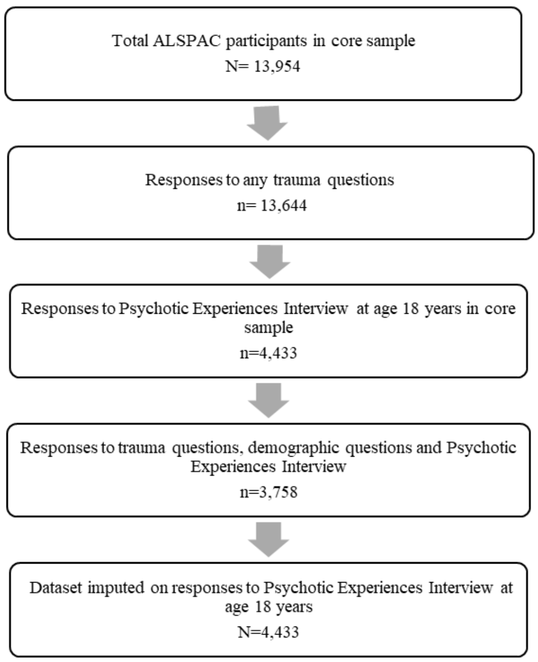
5. To what extent are these relationships explained by confounding?

5.3 Methods

5.3.1 Sample

The analytic sample included Participants from the ALSPAC cohort who attended the PE assessment (PLIKSi) at age 18 years (n=4,433). More detail on the study sample derivation and the ALSPAC cohort is in Chapter 5.

Figure 5.1 Flow Chart of Study I participant inclusion



5.3.2 Measures

This section summarises the measures used in this chapter and Chapter 5 describes methods of assessment for each measure.

5.3.2.1 Psychotic experiences outcomes

Psychotic Experiences at age 18 years: A binary measure of any PEs (none vs definite or suspected PEs) occurring since age 12, as assessed by interview at age 18 years. This measure was the primary outcome in the chapter. The suspected or definite PEs classification includes participants that meet clinical threshold for psychotic disorder.

Psychotic Experiences at age 12 years: A binary measure of any PEs (none vs definite or suspected PEs) occurring in the past 6-months, as assessed by interview at age 12 years. This measure is used for one of the sensitivity analyses to help address reverse causation.

<u>5.3.2.2 Exposure to trauma</u>

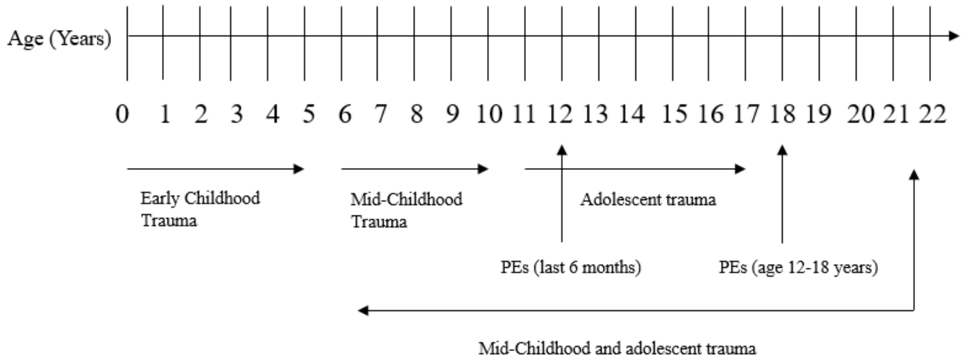
Measures of trauma were derived based on the type of trauma and timing of exposure. In order to answer each research question for study I, I used the following measures of trauma exposure:

Any trauma: A binary measure of exposure to any trauma (physical abuse, emotional abuse, neglect, bullying, sexual abuse, or domestic violence) that occurred (i) anytime between 0-17 years of age, and (ii) during specific age-periods: early childhood (0-4.9 years), mid-childhood (5-10.9 years) and adolescence (11-17 years).

Type of Trauma: Individual binary measures of each trauma type (as listed above) occurring anytime between (i) 0-17 years of age, and (ii) during specific age-periods (early childhood, mid-childhood, adolescence).

Index of trauma exposure dose: Categorical measures of the number of different trauma types reported (0, 1, 2 or 3+) anytime between (i) 0-17 years of age, and (ii) during specific age-periods and a categorical measure of the number of age-periods (0-3) in which exposure to any trauma occurred.

Figure 5.2 Timeline of data collection for trauma and PEs



I used data collected from both parents and children to derive measures of trauma exposure. Only parent-reported data were available for early childhood measures, while measures of trauma in adolescence were predominantly child-reported. As detailed in Figure **5.2**, questions included in trauma measures were collected during age-periods of exposure and at age 22 years.

5.3.2.3 Confounders

Based on prior literature and data availability, I selected and tested the following variables as potential confounders:

Genetic risk for mental health disorder: Polygenic risk scores for schizophrenia, Major Depressive Disorder (MDD), bipolar disorder and neuroticism, and maternal polygenic risk score for schizophrenia.

Socio-Demographic measures: Crowded living conditions, income, socio-economic status, sex, ethnicity, maternal education, maternal smoking during pregnancy, parental drug use, parental trouble with crime

Markers of development: temperament, developmental delay

5.3.3 Statistical Analysis

5.3.3.1 Preliminary Analysis

To confirm that correlation between different types of trauma at each age-period was not substantial enough ($r>0.9$; Kirkwood & Sterne, 2003) to introduce collinear effects to estimations in the main model, I carried out tetrachoric correlation analyses of trauma exposures.

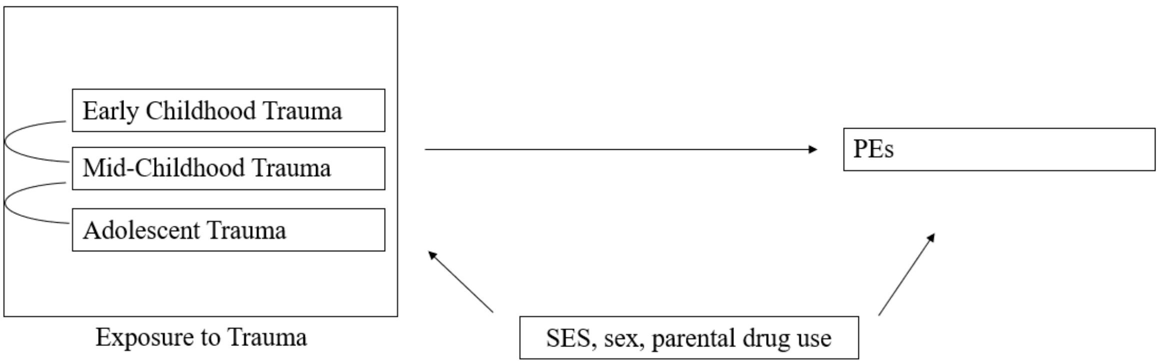
To select confounders for inclusion in the main analysis while maintaining the maximum sample size, I compared unadjusted with individually-adjusted estimates. I only included variables that attenuated the exposure-outcome relationship by 5% or more in the main analytic model as confounders.

5.3.3.2 Main Analysis

I used multivariable logistic regression to assess the relationship between exposure to trauma and PEs at 18 years of age before and after adjusting for the confounders selected from the preliminary analysis (Figure 5.3). I then used multivariable logistic regression that adjusted for trauma-types and confounders.

I used multiple imputation modelling to reduce possible bias from attrition by generating values for missing data for trauma measures and confounders for all participants who completed the PE assessment at age 18 years (n=4,433). Primary results in the chapter are from analyses using the imputed dataset. Results from the complete-case analysis are in Appendix 3 (Appendix Tables 3.3 and 3.4).

Figure 5.3 DAG of analysis of the relationship between trauma and PEs



Using measures of trauma exposure ‘dose’ (number of trauma types, number of age-periods with reported trauma), I tested whether effects were consistent with a dose-response effect. I used likelihood-ratio tests to compare models using linear terms for the exposure with models using categorical terms for the exposure.

I calculated the population-attributable fraction (PAF) using the user-written ‘PUNAF’ command in STATA, but was only able to do this when using complete-case data as the command does not support the use of imputed data (Newson, 2015). This value is the proportion of reduction in an outcome if the exposure was hypothetically reduced to zero (i.e. no trauma exposure) and is calculated based on the assumption that the estimate between trauma and PEs is correctly estimated and wholly causal. For imputed data, I calculated the

PAF values (and confidence intervals) using Levin's classic formula (PAF = p(RR-1) / p(RR-1)+1; Levin, 1953).

5.3.3.3 Sensitivity Analyses

5.3.3.3.1 Information bias

Measures of exposure to physical, emotional and sexual abuse during mid-childhood or adolescence included data collected at age 22 years where participants reported these exposures during earlier age-periods. I tested for potential reporting error by repeating analyses, where possible, using measures of these exposures without data from age 22 years.

As the proportion of parent-reported compared with child-reported measures varied by exposure age-period, there was a potential for informant bias to affect the estimated effect on PEs. Where measures of trauma used data from both parents and children, I repeated analyses using separate measures of trauma reported only by children or only by parents and compared these with each other.

5.3.3.3.2 Potential reverse causation

As the main outcome in my analyses was PEs occurring between ages 12 and 18 years, the results for exposure to adolescent trauma might have been affected by reverse causation if childhood PEs led to an increased risk of exposure to trauma during adolescence. To this address this, I analysed the relationship between exposure to trauma before adolescence (0-10.9 years) and during adolescence (age 11-17 years) and PEs at age 18 years in the sub-sample of participants who did not report definite or suspected PEs at age 12 years.

5.4 Results

5.4.1 Study sample

Compared to ALSPAC participants who were not included in the analyses, those included in the sample were less likely to have a lower socio-economic background, have a history of parental drug use and psychiatric history and were more likely to be female (Table 5.1).

Table 5.1 Sample characteristics of ALSPAC participants who did and did not complete the assessment of the psychotic experiences

Characteristic	Included in sample (n=4,443)[1] N (%)	Not included in sample (n=9,521) N (%)	Odds Ratio	95% CI	P-Value
Female Sex	2,504 (56)	4,245 (45)	1.61	1.50,1.73	<.001
Lowest Income	541 (12)	1,448 (15)	0.50	0.45,0.56	<.001
Maternal education (<O-level)	808 (18)	2,915 (31)	0.41	0.38,0.45	<.001
Living 1+ per room	161 (4)	717 (8)	0.43	0.36,0.51	<.001
Parental Drug Use	393 (9)	914 (10)	0.87	0.77,0.99	0.03
Parental Psychiatric History	722 (16)	1,676 (18)	0.83	0.75,0.91	<.001

Table 5.1 Note: Abbreviation: OR, odds ratio. [1]Participants included in the analytic sample were those who had completed the assessment of psychotic experiences at age 18 years.

5.4.2 Psychotic Experiences

From the total ALSPAC cohort, 4,433 participants attended the assessment of PEs at age 18 years. Of these, 4,078 did not report PEs (92.1%), 167 (3.8%) had suspected symptoms, 113 (2.5%) had definite PEs that did not meet criteria for a disorder, and 75 (1.7%) met the threshold for a clinical disorder.

5.4.3 Exposure to Trauma

As shown in Table 5.2, there were was a substantial proportion of missing data related to exposure to trauma; 60% of participants (n=2,482) in the analytic sample did not have data on trauma exposure across all three age-periods. In the imputed sample, 64.5% of individuals reported exposure to at least one trauma between 0-17 years of age. The estimated prevalence of exposure to trauma was slightly higher in the imputed sample (64.5%) compared to complete-case data (60.8%). Based on imputed estimates, exposure to trauma was more common during mid-childhood and adolescence (38.6% – 43.7%) than during early childhood (22.4%).

In the imputed dataset, 16.8% of the sample were exposed to trauma during more than one age-period, and 37.7% were exposed to more than one type of trauma between 0-17 years of age. The most common type of trauma reported varied during different age-periods. The exposures with the highest prevalence were domestic violence during early childhood

(13.2%), bullying during mid-childhood (21.6%) and physical abuse during adolescence (15.6%). Sexual abuse showed the greatest increase during development: from 0.2% in early childhood to 9.4% during adolescence.

Of those with definite or suspected PEs (n=410, 9.3%) by 18 years of age, 83.8% reported exposure to trauma, compared to 62.6% without PEs.

Table 5.2 Summary statistics of trauma exposure in complete-case and imputed datasets

Trauma type and age-period of exposure	**Proportion of missing data[1] % (n)**	**Frequency of trauma exposure (%)**	
		Observed data	**Imputed data**
Physical Abuse: 0-4.9 years	10.3 (455)	4.6	4.7
Emotional Abuse: 0-4.9 years	10.6 (470)	11.0	11.2
Bullying: 0-4.9 years	11.3 (501)	1.6	1.7
Sexual Abuse: 0-4.9 years	7.3 (324)	0.2	0.2
Domestic Violence: 0-4.9 years	9.5 (423)	12.8	13.2
Any Trauma: 0-4.9 years	**16.8 (744)**	**20.0**	**22.4**
Physical abuse: 5-10.9 years	17.6 (782)	10.2	10.3
Emotional Abuse: 5-10.9 years	16.1 (714)	12.8	12.9
Emotional Neglect: 5-10.9 years	9.34 (414)	3.1	3.5
Bullying: 5-10.9 years	11.03 (489)	21.4	21.6
Sexual Abuse: 5-10.9 years	12.7 (557)	2.7	2.8
Domestic Violence: 5-10.9 years	22.9 (1,013)	11.9	13.1
Any Trauma: 5-11 years	**50.4 (2,236)**	**39.5**	**43.7**
Physical abuse: 11-17 years	19.0 (842)	15.0	15.6
Emotional Abuse: 11-17 years	32.4 (1,434)	9.5	10.0
Emotional Neglect: 11-17 years	4.8 (211)	4.5	3.5
Bullying: 11-17 years	4.5 (201)	15.4	14.4
Sexual Abuse: 11-17 years	35.5 (1,574)	9.9	9.4
Domestic Violence: 11-17 years	24.8 (1,097)	4.2	5.0
Any trauma: 11-17 years	**48.8 (2,164)**	**36.7**	**38.6**
Any trauma: 0-17 years	**60.0 (2,482)**	**60.1**	**64.5**

Note: [1]Number of people with missing data for trauma variable of the 4,433 participants who completed the PLIKSi assessment at age 18 years

5.4.4 Confounders

As detailed in Table 5.3, a higher proportion of participants exposed to sexual abuse were female (87.1%), whereas the distribution of sex for other trauma exposures was more evenly distributed. The distribution of other confounders suggests that participants from a lower socio-economic background more commonly report trauma exposure.

Table 5.3 Distribution of confounders for trauma exposure measure (age 0-17 years)

		N(%) of confounding variable reported in exposed/unexposed trauma groups				
Trauma Exposure Type		**Sex (Female)**	**Parental drug use**	**Living in crowded conditions**	**Low Income**	**Maternal Education (<O level)**
Physical Abuse	Yes	470 (56.3%)	86 (10.4%)	43 (5.4%)	120 (16.0%)	158 (19.6%)
	No	2,027 (56.5%)	307 (8.6%)	118 (3.4%)	421 (13.3%)	647 (18.6%)
Emotional Abuse	Yes	513 (59.2%)	109 (12.7%)	49 (5.9%)	143 (18.0%)	163 (19.2%)
	No	1,979 (55.7%)	284 (8.1%)	110 (3.2%)	398 (12.8%)	640 (18.6%)
Bullying	Yes	597 (49.0%)	102 (8.4%)	53 (4.5%)	151 (13.8%)	242 (20.3%)
	No	1,859 (59.2%)	279 (9.0%)	102 (3.4%)	386 (13.7%)	534 (17.5%)
Sexual Abuse	Yes	303 (87.1%)	33 (9.6%)	16 (4.8%)	58 (18.3%)	166 (48.5%)
	No	2,159 (53.8%)	355 (9.0%)	136 (3.5%)	483 (13.4%)	1,850 (47.4%)
Domestic Violence	Yes	465 (42.7%)	123 (15.3%)	63 (8.2%)	167 (22.9%)	167 (21.4%)
	No	2,011 (56.2%)	264 (7.4%)	93 (2.7%)	374 (11.7%)	626 (18.0%)
Emotional Neglect	Yes	151 (50.0%)	28 (9.3%)	12 (4.3%)	45 (16.5%)	57 (19.4%)
	No	2,291 (57.0%)	848 (8.7%)	141 (3.6%)	483 (13.4%)	716 (8.3%)

5.4.5 Preliminary Analysis

5.4.5.1 Correlation analyses

Correlations between trauma-types at each age-period ranged from 0.01 and 0.72: the highest correlation was between physical and emotional abuse in early childhood (Appendix table 3.1).

5.4.5.2 Confounders

Of the potential confounders tested in the preliminary analysis the following attenuated the relationship between exposure to trauma and PEs at age 18 years by over 5%: sex, parental drug use, income, and maternal education. These variables were included as confounders in the main analysis.

5.5 Main Analysis

5.5.1 Exposure to trauma and risk of subsequent PEs

Exposure to any trauma reported between ages 0 to 17 years was associated with increased odds of PEs at age 18 years (OR_{crude} 3.13; 95% CI: 2.32, 4.22; p<0.001). This estimate was attenuated by <10% when adjusting for confounding (OR_{adj} = 2.91; 95% CI 2.15, 3.93; p<.001).

Based on calculations using Levin's classic formula, the population-attributable fraction for any trauma experienced up to age 17 years on psychotic experiences at age 18 years was 58% (approximate range: 46%-67%). This estimated value was higher than the PAF in the complete-case data using the PUNAF command (45%; 95% CI: 25%-60%).

5.5.2 Trauma type-specific analyses

All trauma types were associated with an increased risk of PEs at 18: the most strongly associated was sexual abuse (OR_{crude} = 2.75; 95% CI: 2.00, 3.79; p<.001) and the least was emotional abuse (OR_{crude}= 1.94; 95% CI: 1.53, 2.46; p<.001). Evidence of these associations was relatively unchanged after adjustment for confounders (Table 5.4). When further adjusting for exposure to all other types of trauma in a multivariable regression model, there was weaker evidence to support a relationship between emotional abuse occurring anytime between 0-17 years of age and risk of PEs (OR_{adj} = 1.25; 95% CI: 0.94-1.65; p=.125). Evidence of an association for all other types of trauma remained strong (ORs = 1.48 – 2.33).

5.5.3 Trauma exposure and risk of PEs according to age-period

The association between exposure to any trauma and increased risk of PEs at 18 years of age was strongest when the trauma exposure occurred during adolescence (OR_{crude} = 2.92; 95% CI 2.29, 3.71; p<.001; Table 5.4) and was weakest when exposure occurred during early childhood (OR_{crude}=1.88; 95% CI 1.49, 2.38 p<.001). The effect estimates for trauma exposure during each age-period were attenuated by confounding variables by between approximately 5-10%; the greatest attenuation was present for exposure to trauma during early childhood.

As the age-period of exposure increased, the association between exposure to domestic violence and PEs became weaker. In contrast, associations for bullying, emotional neglect and sexual abuse became stronger. The largest estimated effect size in analyses of trauma by type and age-period was for exposure to sexual abuse during adolescence (OR_{adj} = 2.34; 95% CI: 1.62, 3.37; p<0.001; Appendix Table 3.2).

Table 5.4 Association between exposure to trauma (age 0-17 years) and subsequent psychotic experiences according to type and age-period[1]

		Unadjusted			Adjusted[2]			Adjusted[2,3]		
	% Exposed	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Any Trauma	64.5	3.13	2.32, 4.22	<.001	2.91	2.15, 3.93	<.001			
Physical Abuse	23.1	2.36	1.85, 3.02	<.001	1.69	1.27, 2.23	<.001	2.24	1.75, 2.87	<.001
Emotional Abuse	23.7	1.94	1.53, 2.46	<.001	1.81	1.42, 2.31	<.001	1.25	0.94, 1.65	0.125
Bullying	32.9	2.07	1.66, 2.57	<.001	2.05	1.65, 2.57	<.001	1.80	1.43, 2.26	<.001
Sexual abuse	11.0	2.75	2.00, 3.79	<.001	2.50	1.79, 3.51	<.001	2.04	1.42, 2.91	<.001
Domestic Violence	21.9	2.02	1.59, 2.56	<.001	1.79	1.40, 2.29	<.001	1.48	1.13, 1.94	0.004
Emotional Neglect	7.8	2.41	1.75, 3.30	<.001	1.89	1.35, 2.65	<.001	2.33	1.70, 3.21	<.001
Trauma (0-4.9 years)	22.5	1.88	1.49, 2.38	<.001	1.70	1.33, 2.17	<.001			
Trauma (5-10.9 years)	43.6	2.27	1.81, 2.84	<.001	2.16	1.71, 2.71	<.001			
Trauma (11-17 years)	40.1	2.92	2.29, 3.71	<.001	2.72	2.13, 3.47	<.001			

[1]Imputed dataset, n=4,433 Abbreviation: OR, odds ratio [2]Adjusted for confounders: sex, parental income, parental drug use, maternal education, crowded living conditions [3]Adjusted for other trauma exposures

Table 5.5 Associations between number of types of trauma and psychotic experiences at 18 years of age[1]

Age-period	N types of trauma (%)	Unadjusted			Adjusted[2]		
		OR	95% CI	*p*	OR	95% CI	*p*
Age 0-17 Years	1 (26.7)	1.94	1.33, 2.81	0.001	1.89	1.30, 2.74	0.001
	2 (16.4)	2.67	1.81, 3.91	<.001	2.54	1.72, 3.75	<.001
	3+ (21.3)	5.19	3.76 7.16	<.001	4.74	3.40, 6.59	<.001
	Linear Trend	1.70	1.54, 1.87	<.001	1.65	1.48, 1.82	<.001
Age 0-4.9 Years	1 (15.4)	1.74	1.31, 2.31	<.001	1.56	1.79, 2.10	.002
	2 (5.4)	2.27	1.54, 3.36	<.001	2.03	1.36, 3.02	<.001
	3+ (1.5)	1.93	.93, 4.02	0.078	1.82	.87, 3.80	0.114
	Linear Trend	1.45	1.26, 1.67	<.001	1.38	1.19, 1.59	<.001
Age 5 – 10.9 years	1 (28.7)	1.80	1.39, 2.34	<.001	1.75	1.34, 2.28	<.001
	2 (10.7)	2.80	2.01, 3.91	<.001	2.65	1.88, 3.73	<.001
	3+ (4.3)	4.33	2.85, 6.57	<.001	3.88	2.53, 5.94	<.001
	Linear Trend	1.65	1.47, 1.85	<.001	1.60	1.42, 1.80	<.001
Age 11 – 17 years	1 (25.9)	2.20	1.66, 2.91	<.001	2.09	1.57, 2.78	<.001
	2 (8.9)	3.47	2.43, 4.94	<.001	3.20	2.23, 4.58	<.001
	3+ (3.8)	7.73	5.12, 11.67	<.001	6.75	4.42, 10.31	<.001
	Linear Trend	1.94	1.72, 2.18	<.001	1.86	1.64, 2.10	<.001

Note: . [1]Imputed dataset, n=4,433 Abbreviation: OR, odds ratio [2]Adjusted for confounders: sex, parental income, parental drug use, maternal education, crowded living conditions

5.5.4 Analysis of trauma dose-response effect on PEs risk

To test whether a dose-response effect was present, I examined whether individuals exposed to a greater number of types of trauma, or those exposed during multiple age-periods, had higher odds of PEs (Table 5.5).Likelihood-ratio tests that compared regression analyses of the number of trauma types as a continuous and a dummy variable were consistent with a linear effect of trauma exposure ‘dose’ on the increased risk of PEs.

I found evidence of a linear increase in the risk of PEs at 18 years of age according to the number of trauma types at both 0-17 years of age (OR_{adj} = 1.65; 95% CI: 1.48, 1.82; p<.001) and during each of the three age-periods of exposure (ORs = 1.45 – 1.94). After adjustment for confounding, the observed linear trends at each age-period were attenuated by approximately 5-10%.

Table 5.6 Associations between the total number of age-periods where trauma was experienced and psychotic experiences at age 18 years[1]

	Unadjusted			**Adjusted[3]**		
Number of age-periods[2] exposed to trauma (%)	OR	95% CI	*p*	OR	95% CI	*p*
1 age-period (27.3%)	1.54	1.19, 2.00	0.001	1.53	1.18, 2.00	0.001
2 age-periods (12.9%)	2.37	1.81, 3.12	<.001	2.29	1.74, 3.02	<0.001
3 age-periods (3.88%)	3.69	2.59, 5.26	<.001	3.45	2.41, 4.95	<0.001
Linear Trend	1.54	1.40, 1.71	<.001	1.51	1.36, 1.68	<0.001

Note: Abbreviation: OR, odds ratio [1]Imputed dataset (n=4,433) Number of age-periods (early childhood/mid-childhood/adolescence) [2]Trauma exposure is reported [3]Adjusted for confounders: sex, parental income, parental drug use, maternal education, crowded living conditions

The greatest increase in the risk of PEs was in those exposed to three or more types of trauma during adolescence (OR_{adj} = 6.75; 95% CI: 4.42, 10.31; p<0.001). I also found evidence of a linear trend for the number of age-periods in which exposure to any trauma was reported and PEs at age 18 years (Table 5.6; OR_{adj} = 1.51 95%; CI: 1.36, 1.68; p<0.001).

5.6 Sensitivity Analysis

5.6.1 Analysis using complete-case data

In the complete-case data analysis, the effect estimate for exposure to any trauma between age 0-17 years and the risk of PEs was lower (OR_{adj} = 2.20; 95% CI: 1.69, 2.86, p<0.001; Appendix Table 3.3) compared to estimates from imputed data (OR_{adj} = 2.91; 95% CI: 2.15, 3.93; p<0.001).

For the analysis of age-specific trauma exposure (detailed in appendices), results were similar to those from imputed data. The main differences were that: i) bullying during adolescence was more strongly associated with PEs in complete-case data (OR_{adj} = 2.77; 95% CI: 1.90, 4.04; p<0.001) than imputed data (OR_{adj} = 1.87 95% CI: 1.45, 2.42; p<0.001), and ii) the effect of sexual abuse on PEs risk was weaker in complete-case data (OR_{adj} = 1.53; 95% CI: 1.06, 2.21, p=0.022) than imputed (OR_{adj} = 2.04 95% CI: 1.42, 2.91; p<0.001). Observations of a dose-response relationship were comparable to results from the imputed data sample (Appendix Table 3.4)

5.6.2 Potential information bias

A potential source of bias is the use of data on trauma exposure during childhood and adolescence collected at age 22 years. As discussed in chapter 4, I did not use data on sexual abuse collected during adolescence as, based on participant responses and questionnaire wording, the data was unreliable. Therefore, I used data collected at age 22 years to inform the measure of sexual abuse during mid-childhood. In the complete-case analysis that omitted questions collected at age 22 years (Table 5.7) the association between exposure to any trauma between 0-17 years and PEs at age 18 years was very similar to the main analysis (OR_{adj} = 2.20; 95% CI: 1.69, 2.86; $p<0.001$).

In complete-case data, children reported a higher level of exposure to trauma (physical abuse, emotional abuse, bullying and sexual abuse in mid-childhood only) in both mid-childhood (21.6% compared to 13.7% by parents) and adolescence (20.2% compared to 7.0% by parents). The correlation between parent-reported and child-reported trauma was low, ranging from 0.20 to 0.31.

To address potential informant bias, I repeated the main analyses using separate measures of trauma reported by parents or children during mid-childhood and adolescence (detailed in Appendix Table 3.6). Effect size estimates were similar for both child-reported trauma and parent-reported trauma and PEs.

Table 5.7 Associations between trauma and psychotic experiences at age 18 years old exposures omitting trauma data collected at age 22 years[1]

		Unadjusted			**Adjusted[2]**		
Age-period		**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
5-10.9 years	Physical Abuse	1.48	.88, 2.47	0.136	1.55	.92, 2.61	0.100
	Emotional Abuse	1.70	1.22, 2.36	0.002	1.70	1.22, 2.37	0.002
	Sexual Abuse	0.70	.08, 5.61	0.736	0.47	.06, 3.78	0.476
	Any Reported Trauma	1.55	.91, 2.64	0.109	1.74	1.34, 2.27	<0.001
11-17 years	Physical Abuse	3.20	2.2, 4.65	<0.001	3.02	2.06, 4.46	<0.001
	Emotional Abuse	1.83	1.12, 3.01	0.017	1.74	1.06, 2.87	0.030
	Any Reported Trauma[3]	2.12	1.65, 2.69	<0.001	1.96	1.52, 2.52	<0.001
0-17 trauma	Any Reported Trauma[3]	2.62	2.02, 3.41	<0.001	2.25	1.68, 3.02	<0.001

Note: Abbreviation: OR, odds ratio [1]The following categories included were derived using a number retrospective questionnaires at 22 years old and data from these questions are omitted in this analysis: 5-10.9

years: physical abuse, emotional abuse, sexual abuse, 11-17 years: physical abuse, emotional abuse, sexual abuse [2]Adjusted for confounders: sex, parental income, parental drug use, maternal education, crowded living. [3]This measure does not include sexual abuse as the measure for this at this age was derived from the age 22 questionnaire only

5.6.3 Recency effects

In the main analysis, I found evidence of an increased effect of trauma during adolescence on PEs at age 18 years compared to earlier age-periods. Therefore, I wanted to test if there was evidence of a ‘recency’ effect for more recent trauma (age 5-10.9 years) on the risk of PEs at age 12 years compared to a more distal measure of exposure to trauma at (age 0-4.9 years). Exposure to trauma in mid-childhood was more strongly associated with psychotic experiences at age 12 years (OR_{adj} =1.80; 95% CI: 1.45, 2.16; p<0.001) than exposure to trauma in early childhood (OR_{adj} = 1.33; 95% CI: 1.08, 1.65; p=0.008), although the confidence intervals overlapped.

5.6.4 Potential reverse causality

In the sub-sample of participants who did not report PEs at 12 years (imputed n=3,799; Table 5.8), exposure to trauma during adolescence was associated with PEs at age 18 years (OR_{adj} = 2.18; 95% CI = 1.62, 2.93; p<0.001). Exposure to any trauma before adolescence (0-10.9 years) was associated with an increased risk of PEs at age 18 years (OR_{adj}= 1.82; 95% CI: 1.38, 2.38; p<0.001). There was weaker evidence that sexual abuse or emotional neglect that occurred prior to adolescence (0-10.9 years) were associated with an increased risk of PEs at 18 years. Other types of trauma included in the model were of similar effect size to the main model.

Table 5.8 Associations between trauma in adolescence[1] and psychotic experiences at 18 years, excluding psychotic experiences at 12 years[2,3]

	Unadjusted			**Adjusted[4]**			**Adjusted[4,5]**		
Category	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Physical Abuse	2.65	1.89, 3.73	<.001	2.43	1.71, 3.47	<.001	1.96	1.33, 2.98	0.001
Emotional Abuse	2.07	1.20, 3.28	0.002	1.89	1.18, 3.00	0.008	1.25	.74, 2.12	0.402
Bullying	1.87	1.34, 2.62	<.001	1.80	1.29, 2.52	0.001	1.62	1.15, 2.30	0.006
Sexual Abuse	3.00	1.98, 4.53	<.001	2.77	1.81, 4.25	<.001	2.19	1.40, 3.43	0.001
Domestic Violence	1.49	.73, 3.03	0.274	1.21	.59, 2.49	0.605	.98	.46, 2.10	0.967
Emotional Neglect	1.37	.72, 2.61	0.331	1.34	.70, 2.56	0.375	1.16	.60, 2.27	0.656
Any reported trauma	2.37	1.77, 3.17	<.001	2.18	1.62, 2.93	<0.001			

Note: Abbreviation OR, odds ratio [1]Trauma Reported between age 11 – 16.9 years [2]Imputed dataset (n=3,799) [3]Participants who reported definite or suspected psychotic experiences at 12 years old were excluded from analysis [4]Adjusted for confounders: sex, parental income, parental drug use, maternal education, crowded living [5]Adjusted for exposure to other types of trauma

5.7 Discussion

5.7.1 Main findings

Exposure to trauma during childhood and adolescence was associated with an increased risk of having PEs at age 18 years. Effect sizes were similar for different types of interpersonal violence and neglect. For the analysis of age-period effects, there was some evidence of a stronger effect for exposure to trauma in adolescence on PEs compared to earlier age-periods.

The estimated PAF from imputed and complete-case samples (45% - 58%) is comparable to the PAF of 33% (95% CI 16% - 47%) reported by Varese and colleagues (2012). Based on the assumption that the effect of trauma on the risk of PEs is causal and that estimates are not biased, the PAF suggests that a large proportion of participants would not have developed PEs by 18 years of age had they not been exposed to childhood trauma.

5.7.2 The role of confounding in the relationship between trauma and PEs

One of the main aims of the chapter was to establish to what extent the association between exposure to trauma and an increased risk of subsequent PEs was accounted for by confounding. After adjustment for confounding, participants exposed to trauma between age 0-17 years were approximately 3-times more likely to report PEs than those not exposed to trauma. The small attenuation (5-10%) in estimates observed after adjusting for several confounders - including sex, developmental delay, increased genetic risk of psychopathology and several measures of socio-economic status - support the view that the relationship between trauma and PEs is not due to environmental or genetic confounders. This finding is consistent with previous studies that did not observe substantial attenuation in observed effects having adjusted for potential confounders including socioeconomic status and genetic risk of schizophrenia (Arseneault et al., 2011; Lataster et al., 2006; Nierop et al., 2014; Varese et al., 2012).

5.7.3 Type of trauma exposure and PEs

Results from the chapter support the hypothesis that different types of interpersonal violence and neglect during childhood and adolescence are associated with an increased risk of subsequent PEs. The lack of evidence for a differential effect of exposure to different types of interpersonal violence and neglect on PEs is consistent with previous studies that have reported overlapping confidence intervals for different types of traumatic exposure (Arseneault et al., 2011; Kelleher et al., 2013; Spauwen et al., 2006; van Nierop et al., 2014; Varese et al., 2012) and is contrary to claims that specific types of trauma are differentially associated with psychosis-related outcomes (Abajobir et al., 2017; Bentall et al., 2012). This finding suggests that the experience of extreme distress resulting from different types of violence and neglect may commonly contribute to an increased risk of PEs irrespective of the context or content of the trauma exposure.

As exposure to multiple trauma types was common in this sample, as has been observed in other cohort studies (Copeland et al., 2018; Fisher et al., 2015), it is difficult to tease apart the independent effects of different trauma types. Results from the correlation analysis of trauma types at each age-period do not suggest that collinearity would have led to problems with my regression analyses. Indeed, there wasn't a substantial increase in any of the standard errors in my regression analyses that would indicate problematic levels of collinearity. The use of multivariable logistic regression to control for the effects of other trauma types suggests that all types of trauma exposure between ages 0-17 years are independently associated with PEs, with the possible exception of emotional abuse. Confidence intervals for estimates of emotional abuse did overlap with estimates of other trauma types and risk of PEs, which does suggest that the effects are comparable despite a smaller estimated effect size. It may be that emotional abuse was subject to greater measurement error than other measures of trauma. For example, emotional abuse may require more insight for parents and children to recognise compared to acts of victimisation.

Few studies have used multivariable modelling to control for the effect of other trauma types when making inferences about trauma-specific effects, which limits comparison with previous literature. In a large international cross-sectional study, results suggested that forms of violence were independently associated with PEs after controlling for confounders (age, sex, country) and other types of trauma exposure (McGrath et al., 2017). Furthermore, McGrath and colleagues' findings did not provide evidence that other forms of trauma (near-death experiences, natural disasters, death of a loved one) are associated with PEs after adjusting for exposure to violence. McGrath and colleagues' findings are consistent with the findings in this thesis, which suggest forms of interpersonal violence and neglect are independently associated with an increased risk of PEs. However, McGrath and colleagues did not collect data on exposure to neglect or emotional abuse or adjust for socio-demographic confounders, which limits comparability with my findings to some extent.

The overall estimate of the association between exposure to domestic violence between ages 0-17 years and PEs was weaker compared to the other types of trauma analysed. While there was a strong association between exposure to domestic violence and the risk of PEs during early childhood, the strength of this association declined in subsequent age-periods. These results may be due to environmental changes during development; children may be exposed to greater adverse effects and chronic stress from domestic violence in earlier years before they enter the school system. In later years, children may gain sources of protection, such as peer support or wider community networks outside the home that could buffer the effect of domestic violence on PEs. To my knowledge, previous studies have not investigated the effect of exposure to domestic violence on PEs risk during different age-periods in childhood and adolescence.

5.7.4 Age-period of trauma exposure and PEs

The results suggest that exposure to trauma at any age-period during childhood and adolescence is associated with an increased risk of later PEs. I did find some evidence to suggest that the risk of PEs is slightly greater following exposure to trauma during adolescence compared to early childhood or mid-childhood. However, confidence intervals between estimates from trauma from different age-periods overlapped substantially and, therefore, do not provide strong evidence of differential effects of trauma according to age-period. These findings do not suggest that there is a critical or sensitive period of risk for exposure to trauma during development on the risk of subsequent PEs.

As discussed in the introduction, previous studies also report overlapping confidence estimates for trauma exposure at different age-periods (Arseneault et al., 2011; Spauwen et al., 2006). There are key differences between this current study and these previous studies, which does limit any comparison. Arsenault and colleagues (2011) compared different age-periods up to the age of 12 years and, therefore, did not analyse adolescent trauma exposure. Spauwen and colleagues (2006) did not analyse exposure to peer victimisation, which is a significant source of traumatic exposure during development. These variations in measurement suggest that findings from neither study are directly comparable with the results in this chapter.

5.7.5 Recency effects

In the main analysis, I found that exposure to trauma during adolescence was associated with a greater increase in the risk of PEs compared to earlier age-periods. I therefore considered, and tested in further analyses, whether this observation could be accounted for by the proximity of the timing of the exposure to the timing of PE assessment.

When comparing the estimated effect sizes between exposure to trauma during early childhood and mid-childhood and subsequent PEs at age 12 years, I found a slightly elevated estimated effect for more recent trauma exposure compared with the more distal one. This finding is consistent with the argument that the proximity between the timing of exposure and assessment may be more important than exposure during a specific developmental period. However, the interpretation of these results as evidence of a recency effect is limited by overlapping confidence intervals between the estimates for exposure to trauma during early childhood and mid-childhood with PEs at age 12 years. A recency effect may occur as a result of an increased risk of PEs during a short-term response to traumatic stress (for example due to transient biological changes – see discussion Chapter 8), which recedes over time if an individual is not exposed to further trauma. This finding is consistent with Kelleher and colleagues' (2013) finding that for participants who report bullying at baseline but not at later timepoints, the risk of PEs is lower compared to those who experience persistent bullying.

5.7.6 Dose-response effect of trauma exposure

One of the main aims of this chapter was to investigate whether a dose-response relationship exists between trauma exposure and increased risk PEs. I found evidence to support a dose-response effect using indices of both the number of different types of trauma reported and the number of age-periods during which exposure to trauma occurred. A substantial proportion of the study sample (37.7%) reported exposure to two or more types of trauma, and 15.7%

reported exposure to trauma during at least two age-periods. As with previous studies, there was evidence of a dose-response effect of trauma on PEs (Arseneault et al., 2011; Bentall et al., 2012; De Loore et al., 2007; McGrath et al., 2017; Moriyama et al., 2018; Shevlin et al., 2008). The dose-response effect was present according to exposure to multiple types of trauma and during multiple age-periods.

These results suggest that exposure to multiple types of trauma are associated with a greater increase in the likelihood of later PEs than exposure to a specific type of trauma or during a specific period of development. As a linear increase in the risk of an outcome according to the frequency of exposure is one of Hill's (1965) criteria for causality, my findings can be interpreted to support the thesis that the relationship between trauma exposure and subsequent PEs is causal.

Participants exposed to more than one type of trauma may be at an increased risk of being exposed to trauma in different environmental contexts, for example at home and at school, which could reduce the availability of protective environmental factors compared to individuals exposed to trauma in a single environmental context. For children exposed to multiple types of trauma, social support can have a protective effect on the risk of PEs (Crush et al., 2018); such support may be more difficult to find where poly-victimization across multiple environmental contexts is present. These results suggest that exposure to multiple forms of trauma is associated with the greatest increase in the risk of PEs compared to exposure to any single type of trauma.

5.7.7 Potential reverse causality

I also attempted to reduce the risk that the effects for exposure to trauma during adolescence observed in the main analysis were due to reverse causation by excluding participants who were rated as having PEs at age 12 years from the main analysis. Evidence of association between exposure to trauma during adolescence (age 11-17 years) and PEs at age 18 years was also present in the sub-group of participants who did not report PEs at age 12 years. This finding suggests that reverse-causality does not account for the results observed in the main analysis.

This finding is in line with findings by Lataster and colleagues (2012) who found some evidence of an association between exposure to trauma and the risk of subsequent PLEs in a large cohort after excluding participants who reported PLEs at baseline (n=427; RR 1.68 95% CI 1.03-2.72 p=0.038). After adjusting for baseline PLEs, studies have reported an association between trauma and PLEs (De Loore et al., 2007; Janssen et al., 2004; Mackie et al., 2013). However, adjustment for baseline symptoms is a less robust method to eliminate potential reverse causation compared to omitting participants from analyses; therefore, results from these studies are not directly comparable.

5.7.8 Strengths and Limitations

The study benefitted from a rich dataset of questions relating to exposure to different types of trauma at multiple age-periods reported by both parents and children. I was able to investigate several research questions relating to the relationship between timing and type of trauma exposure and the risk of PEs. The use of rater reports of PEs from validated, semi-structured interviews strengthens the validity of results in this chapter. As discussed in Chapter 1, measures of PEs and PLEs vary greatly in previous literature and are often liable to measurement error, therefore investigating trauma and PEs using a reliable measure of PEs addresses current limitations to the evidence base. I was also able to investigate potential reverse causation by excluding individuals with PEs at an earlier age-period (age 12 years) in sensitivity analyses, which increased confidence of a temporal relationship between trauma and PEs.

The availability of both environmental and genetic measures to test as potential confounders was also a key strength for analyses in this chapter. To my knowledge, this is the first study to include several confounders in analyses of trauma and PEs including genetic risk for psychopathology (depression, bipolar disorder, neuroticism, and schizophrenia) and early-life behavioural markers (developmental delay and temperament). The use of multiple measures of socioeconomic status in early life (average income, social class, crowded living conditions) and adverse environmental factors (parental history of mental health, parental drug use) enabled me to test environmental factors as a potential source of confounding comprehensively. By establishing that these confounders do not substantially attenuate the relationship between childhood trauma and subsequent PEs, the results strengthen the assertion that the relationship is causal.

I was also able to address possible bias from attrition. I used multiple imputation to predict missing values using a range of auxiliary variables (e.g. markers of social disadvantage and poor mental health) that were associated with missingness and with my exposures and outcomes of interest. Using multiple imputation, I was able to carry out analyses in a sample that is less likely to be affected by attrition bias than a complete-case sample.

There are some limitations related to the measurement of trauma in this study. As the study did not use a standardised measure of trauma, the replicability and generalisability of the results are limited when comparing these to results from other cohort studies. While I made every effort to ensure that trauma questions included in the binary measure of trauma referred to exposure to extreme instances of stress, measurement error may bias the observed results. As it is likely that this source of measurement is not differential according to PEs status, this most likely leads to an underestimation of the effect of trauma on PEs.

Correlation between the trauma variables was low enough for collinearity to not play an instrumental role in the study. It was difficult to tease apart the specific effects of single types of trauma and specific age-periods when a large proportion of participants reported exposure to exposure to multiple types of trauma and during multiple age-periods. Penalised regression methods and life-course modelling approaches, such as the least absolute shrinkage and selection operator (LASSO) and structured life course modelling (SLCMA), may have offered a more rigorous method of examining trauma-type-specific and timing of exposure effects than multivariable regression modelling (Dunn, Crawford, et al., 2018; Tibshirani, 1996). However, this method was considered not feasible at the time of analysis using imputed data and a binary outcome (Wood et al., 2008).

As is common in longitudinal studies, there was a high proportion of missing data as the exposures recorded are based on multiple assessments. The estimated prevalence of trauma and the effect of trauma on PEs was consistent between complete-case and imputed data. This finding suggests that the complete-case sample is less likely to be substantially affected by attrition bias.

I aimed to address issues relating to missing data and used imputation methods to predict missing values for the sample that completed the PEs assessment (32% of the ALSPAC cohort). However, this method does not address the demographic differences between participants in the ALSPAC cohort who did and did not attend the PEs assessment. The sample that did attend the PEs assessment were more likely to be from a higher socio-economic background compared to those that did not complete the assessment. As a lower socio-economic background is associated with a greater likelihood of exposure to trauma, it is likely that the estimated effects of trauma on the risk of PEs in this sample are underestimated compared to a more representative sample from the general population.

As described in the methods section, I used measures of exposure to trauma based on both reports of trauma from parents and children. Parental underreporting may lead to measurement error of trauma in early childhood and differences in subjective assessments of trauma exposure that may not be accurate. However, based on the results of the sensitivity analysis, there was a lack of notable difference in effect size estimates according to the data source for parent-reported and child-reported trauma at later age-periods, which do not suggest this was a problem.

As a recent meta-analysis has reported, there is a low agreement between reporting of trauma at different timepoints (e.g. during childhood and later in adulthood; Baldwin et al., 2019). In a further sensitivity analysis, I omitted measures of trauma collected at age 22 years that referred to trauma exposure during mid-childhood and adolescence. Results from this analysis were in line with my main analysis and, therefore, suggest that the timing of trauma assessment did not affect estimated effect size.

5.7.9 Implications

While there are limitations for inferring causality from observational studies, my results are consistent with trauma having a causal effect on PEs. The results also highlight that trauma during every age-period is associated with an increased risk of PEs. These findings, of both a high prevalence of trauma exposure and a consistent association with subsequent PEs, support the need to consider young people’s vulnerability to trauma during both childhood and adolescence and its impact on the risk of psychopathology. As the relationship between trauma and an increased risk of subsequent PEs was observed during different age-periods and in analyses of several types of interpersonal violence and neglect, the results of this chapter suggest that the effect is consistent and is likely to be causal.

Based on the implication of the results that the relationship between exposure to trauma and PEs is causal, these findings support the need for further studies to investigate mechanisms on this pathway. Investigation of potential mediators on the pathway from trauma to subsequent PEs using longitudinal studies is needed. These findings can contribute to a unified model of psychosis that can describe mechanisms that contribute to the development of PEs on biological, psychological and cognitive levels of explanation.

There is evidence that PEs are associated with the presence of, and with increased risk of developing, a wide range of adverse mental health outcomes including common mental health disorders and suicidality (Fisher et al., 2013; Healy et al., 2019; Linscott & Os, 2013). Therefore, studies of mechanisms on the causal pathway from trauma to PEs may have implications for non-psychotic psychiatric outcomes.

My findings support the argument that reducing exposure to trauma during childhood is a public health priority as it is associated with a wide range of negative mental, physical and social outcomes (Dale et al., 2014). Meta-analyses provide evidence that interventions can reduce bullying in schools (Jiménez-Barbero et al., 2016; Ttofi & Farrington, 2011), which, based on my findings and the current evidence base, may prevent cases of PEs. However, there is evidence that intervention for other types of trauma is less effective. Results from a meta-analysis estimate that the effect of interventions aimed at reducing child maltreatment and exposure to domestic violence are small (van der Put et al., 2018; Vlahovicova et al., 2017). Pooled analysis suggests that there is a lack of evidence to suggest the use of school-based interventions to reduce exposure to dating violence during adolescence (De La Rue et al., 2017). As prevention of childhood trauma is not achievable for a large proportion of the population, identifying interventions that can mitigate the risk of PEs for those exposed to trauma may be a more effective approach to preventing PEs.

Routinely screening individuals exposed to interpersonal trauma for PEs, particularly individuals exposed to chronic and frequent trauma, to improve their early detection and prevent adverse outcomes (Davies et al., 2018; McGrath et al., 2016; Sharifi et al., 2015) seems warranted and requires evaluation. The findings from this chapter also support the need for future studies to investigate protective factors that prevent the development of PEs in the large proportion of young people who are exposed to trauma.

5.8 Conclusion

The results of this chapter provide evidence of a dose-response association between exposure to trauma and an increased risk of PEs. This relationship was not accounted for by confounding from environmental or genetic risk factors, or due to reverse causation, measurement bias or selection bias. These results, therefore, support the argument that there is a causal relationship between exposure to trauma and PEs. However, there was little evidence to suggest that the association between trauma exposure and PEs is specific to the type of interpersonal violence or neglect exposed to, or that critical or sensitive age-periods of exposure exist.

Chapter 6. Study II: A Systematic Review and Meta-Analysis of Childhood Trauma and Cognitive and Perceptual Biases Associated with Psychosis

6.1 Overview

This chapter presents a systematic review and meta-analysis of studies that have investigated the relationship between exposure to childhood trauma and cognitive and perceptual biases associated with psychosis. The aims of the review are informed by theories that childhood trauma and cognitive biases lie on a causal pathway to the development of psychotic symptoms and that empirical evidence suggests that trauma and cognitive and perceptual biases are associated with an increased risk of psychotic symptoms (Chapter 2).

6.2 Background

As summarised in Chapter 1, there is a body of evidence that supports the hypothesis that exposure to childhood trauma is associated with an increased risk of psychotic symptoms in both clinical and sub-clinical contexts and, based on results from Chapter 5, is likely to be causal. However, there is limited knowledge of the mechanisms that underlie this relationship. There is a need to develop current knowledge of the mechanisms that lie on the theorised causal pathway from trauma to psychotic symptoms to identify targets for preventative interventions.

Integrated neuro-developmental models of psychosis hypothesise that the neurobiological consequences of stress, including disruption in the hypothalamic-pituitary-adrenal (HPA) axis, trigger cognitive and perceptual biases associated with an increased risk of psychotic symptoms (Howes & Kapur, 2009). Theses biases are potential mechanisms to account for the increased risk of psychotic symptoms from exposure to trauma.

In a variety of tasks, cognitive and perceptual biases are associated with psychosis-related outcomes. These tasks include how individuals make decisions, estimate the likelihood of an event and disambiguate new information. As will be outlined in this chapter, these biases have been tested empirically using a range of paradigms.

While it is hypothesised that exposure to chronic stress triggers cognitive and perceptual biases associated with psychotic symptoms, it is largely unknown whether trauma increases the likelihood of these cognitive and perceptual biases. If trauma is associated with an increased likelihood of cognitive and perceptual biases associated with psychosis, these biases may be indicators of vulnerability to psychotic symptoms and could inform preventative interventions.

6.2.1 Summary of cognitive and perceptual biases included in the review

There is a range of cognitive and perceptual biases that are associated with psychosis and are potentially associated with trauma. The biases reviewed can be broadly categorised into three categories: (i) estimations of agency and causality, (ii) methods of inference and belief-updating and (iii) methods of perceiving new information. I will briefly summarise these categories.

Estimations of agency (locus of control; LOC), and attributions of causality (attribution bias), are associated with negative mental health outcomes. A more external LOC is a bias towards attributing control to external forces, including fate and chance. Consequently, an external LOC indicates a diminished sense of self-efficacy and is associated with a vulnerability to negative mental health outcomes, including psychotic symptoms (Thompson et al., 2011). LOC is measured using various self-report measures relating to attitudes and beliefs.

Attribution theory states that individuals interpret the cause of negative events according to three different situational scales. These scales are whether the cause of an event is: (i) particular to a situation or are relevant in different situations (local or global), (ii) temporary or persistent (unstable and stable) and (iii) due to personal actions or the actions of others (internal or external; Holder & Levi, 1988). Symptoms of psychosis are associated with a greater likelihood of identifying a negative event as caused by global, stable and external situational factors (Freeman, 2007; Kaney & Bentall, 1989). A bias for attributing the cause of negative events to others, an external attribution bias, is associated with symptoms of schizophrenia (An et al., 2010). Assessment for the bias involves participants rating the attribution of cause in a series of hypothetical events.

Methods of belief-updating and inference have been used to measure biases that are hypothesised to facilitate the development of erroneous beliefs that may contribute to delusions. In the probabilistic reasoning paradigm, participants are asked to decide on the most probable outcome in a scenario and test how much information is required before an individual makes this decision. Making a decision based on minimal information is defined as the ‘Jumping to Conclusions’ (JTC) bias that is associated with symptoms of psychosis (Dudley et al., 2015; Ross et al., 2015). The JTC bias is theorised to contribute to the development of delusions by supporting the quick adoption of implausible beliefs.

In contrast to the JTC bias, a bias against disconfirmatory evidence (BADE) tests how resistant individuals are to contradictory evidence once they have adopted a belief. The BADE task paradigm presents individuals with information about a scenario and asks them to rate the plausibility of these scenarios before and after receiving additional statements, some of which appear to contradict previous information. Being resistant to revising estimations after receiving contradictory information in this context is associated with psychotic symptoms (Eisenacher et al., 2016; Woodward et al., 2008). The assessment involves participants rating the plausibility of a scenario before and after receiving contradictory evidence.

How individuals perceive new information can indicate biases that contribute to abnormal perceptual experiences. The ability to identify whether stimuli are self-generated (e.g. speech or thought) or from an external source (e.g. a person or computer), is referred to as source monitoring. A bias for identifying self-generated information as externally generated in source monitoring tasks is associated with psychosis-related outcomes. Cognitive models suggest that a bias towards attributing self-generated actions or speech to external sources is an underlying mechanism for the development of hallucinations (Brookwell et al., 2013, 2013; Griffin & Fletcher, 2017). In perceptual tasks, the overreliance on prior expectations when perceiving new information (‘top-down’ processing), over immediate sensory data, (‘bottom-up’ processing), is associated with hallucinations (Daalman et al., 2012; Schmack et al., 2015; Teufel et al., 2015).

6.3 Chapter Aims and Research Questions

This chapter uses a systematic review and meta-analysis to examine whether exposure to trauma before age 18 years is associated with biases that have previously been found to be associated with psychosis (as listed in Section 6.4.4.1).

6.4 Methods

6.4.1 Development of Search Criteria

Based on the earlier literature review (Chapter 3) and scoping searches, I identified potential biases that would be suitable to include in the review. In my search, I initially included the hostile attribution bias, a bias to interpret neutral situations as threatening, as part of the search criteria as it is associated with psychotic symptoms (Pot-Kolder et al., 2018). I found that the association between exposure to trauma and this bias had been the subject of a recent systematic review and meta-analysis (da Silva Ferreira, Crippa, & de Lima Osório, 2014). Based on this, I did not include the hostile attribution bias in the search criteria.

Once I had identified the biases to include in the search, I developed criteria for the systematic review using previous systematic review methods and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidance (Moher, Liberati, Tetzlaff, Altman, & Group, 2009). I decided to include only English-language studies published in peer-reviewed publications. I also decided to restrict the age of exposure to trauma to have occurred before age 18 years so that the review would inform studies of exposure to childhood trauma and psychotic symptoms.

6.4.2 Pre-Registration of Study

The protocol for the study was pre-registered on the PROSPERO database (ID: CRD42017059401; see supplementary) and was later revised to omit the hostile attribution bias as a bias included in the search criteria.

6.4.3 Identification of Studies

I searched PsychInfo, OVID Medline® and PILOTs for relevant studies up to 18th October 2017. The keywords used were trauma-related terms (trauma, maltreatment, adversity, neglect, bully, victim, rape, violence, assault) and terms related to biases (e.g. locus of control, attribution style, JTC bias, source monitoring). The full list of search terms used for each of the three databases are listed in Appendix Figure 4.1. I then screened abstracts to select studies that were suitable for a full-text screening using Rayyan (Ouzzani, Hammady, Fedorowicz, & Elmagarmid, 2016), an online tool for screening abstracts.

6.4.4 Selection Criteria

Studies were included if they met the following criteria: (i) published, in English, in a peer-reviewed journal, (ii) tested a bias (or biases) described in search criteria (below), and (iii) compared performance on tasks between participants exposed to trauma before 18 years of age and those who did not.

Trauma was defined as exposure to accidental or intentional harm that is outside of everyday experience and includes victimisation, sexual abuse, emotional abuse and neglect. The criteria for exposure to trauma did not include exposure to adverse experiences such as family instability, economic adversity or parental substance use. This definition was used to identify stressors that would be considered as traumatic to understand their specific effects on information-processing biases during development.

6.4.4.1 Measures included in the search

The study search included studies that measured the following biases:

- External LOC
- External attribution bias
- The JTC bias
- Bias against disconfirmatory evidence
- Top-down processing bias
- External source monitoring bias

These biases are summarised in section 6.2.1 and Chapter 3.

6.4.5 Study Selection and Data Extraction

After I had screened abstracts and obtained full texts of studies that were potentially suitable for inclusion, a second reviewer and I assessed full texts to see whether they fulfilled the inclusion criteria described in section 6.4.4 (see Screening checklist Appendix Figure 4.2).

Data were extracted from all included papers by both a co-reviewer and I to minimise error. The following information from the studies was extracted: country of origin, study setting, design, sampling strategy, sample size, mean age, type(s) of trauma exposure assessed, proportion exposed to trauma, biases assessed, reported results and adjustment for any confounders. A third reviewer resolved any differences between reviewers in screening and data extraction.

6.4.6 Quality Assessment

I reviewed several methods available for assessing the quality of observational studies in systematic reviews and selected the Newcastle-Ottawa scale (Wells, Shea, Peterson, Welch & Losos, 2009; Appendix Figure 4.3) as the most suitable tool to meaningfully assess study quality; this was based on the tool having appropriate categories to assess aspects of quality and potential sources of bias relevant to observational studies that use cross-sectional data. I was also able to further adapt the tool by only including items relevant to the review to ensure that the quality assessment was as concise as possible.

Studies were rated based on the presence or absence of the following criteria: i) Random or complete sampling (1 point), ii) Response rate of 75% or more (1 point), iii) Non-exposed sample representative of exposed sample (1 point), iv) Adjustment for confounders (max. 2 points), and v) Observer bias minimised (1 point). Total scores were calculated by summing scores across these five criteria (possible score 0-6)

I identified the method of recruitment in studies as a potential source of bias. Complete or random sampling refers to sampling from the entirety of a population that is eligible to be included, such as a school cohort or a hospital ward, and all participants have an equal chance of being included in the study. In convenience sampling, members of a population have an unequal chance of being recruited to the study, such as using advertising methods that only target a small sample of a population, which potentially introduces selection bias.

The search criteria did not specify the study population; therefore, quality assessment focused on the extent to which non-exposed participants were representative of the exposed group. In studies where study groups were drawn from separate populations, I assessed to what extent the participants were drawn from similar populations and what demographic information was reported in the study to inform this.

The extent to which studies adjusted for potential confounding factors is a key component of the quality of the studies included in the review. Adjusting for confounding factors can increase the comparability between groups and highlight any factors that may attenuate or account for the association between trauma and the bias of interest. I selected, *a priori*, variables that I consider potential confounders of the relationship between trauma and the biases of interest: sex, markers of cognitive functioning (e.g. IQ), socio-economic status and age. The scale was adapted to reflect these chosen confounding variables.

Methods of assessing cognitive biases are also a source of potential study bias. If the assessors of the cognitive or perceptual bias are aware of the exposure status of the participant, this may bias the conduct of the assessment. Studies that used methods that minimised observer bias were assessed as higher quality.

6.4.7 Assessment of publication bias

I assessed potential publication bias by conducting an Egger's regression test (Egger et al., 1997). The Egger's test performs a linear regression of the effect estimates on their standard error measurement to estimate the extent to which the pooled analysis deviates from a funnel-plot distribution. This analysis was conducted using the 'metabias' command in STATA.

6.4.8 Data Analysis

After finalising the studies for inclusion in the review, I assessed the feasibility of using meta-analysis for the included studies. Based on the number of included studies for each bias, only a meta-analysis of LOC studies was feasible. As a range of scales were used to assessed LOC, I standardised LOC scores using the following data: the number of exposed and non-exposed participants and the mean LOC score and standard deviation for each group. This information was used to calculate the standard mean difference (SMD) of the LOC score for each exposed and non-exposed group in each study, where a higher score denoted a more external LOC. For studies where exposed groups were separated according to different categories, such as trauma type or severity, I combined means and standard deviations according to Cochrane guidelines (Higgins et al., 2008).

To accommodate the heterogeneity between sample populations and scales used to assess the LOC, I conducted a random-effects meta-analysis using the 'metan' command in STATA version 15. Heterogeneity was assessed using the I^2 statistic. Using meta-regression (the 'metareg' command in STATA), I assessed whether likely sources of variation (study quality, recruitment sample (e.g. clinical, general population), mean age, and sex distribution of sample) explained any heterogeneity.

Where sufficient data were not available to conduct a meta-analysis, a narrative synthesis was used to review studies.

6.5 Results

Eighty-one articles were reviewed in full and assessed for eligibility according to the inclusion criteria. After reading the full texts, 56 full articles were excluded (Figure 6.1). Twenty-five studies were included as they fulfilled all search criteria.

6.5.1 Characteristics of included studies

Included studies were based in the following countries (Table 6.1): USA (12 studies) UK (3 studies) Australia (2 studies) and one each in Canada, Greece, Holland, Italy, Japan, New, Turkey and Taiwan.

Six studies (Barahal et al., 1981; Bendall et al., 2011; Mannarino & Cohen, 1996; Moran & Eckenrode, 1992; Moyer et al., 1997a; Roazzi et al., 2016) recruited separate exposed and unexposed samples, and the remaining studies sampled subpopulations that contained both exposed and unexposed groups. Twelve studies recruited participants who were less than 18 years of age, 12 recruited participants over 18 years of age and 1 study sampled participants across this age threshold. Four studies assessed exposure to trauma based on referrals from child protection authorities and all other studies used self-report measures of trauma using a range of self-report questionnaires relating to different types of trauma (Appendix Table 4.1).

Twenty-four studies examined only one type of information processing bias. One study (Mannarino & Cohen, 1996) examined both LOC and external attribution bias, contributing two results to the review. No studies were included in the search that examined a bias for relying on top-down knowledge to disambiguate new information or a bias against disconfirmatory evidence.

Figure 6.1 Flow chart of the review screening process

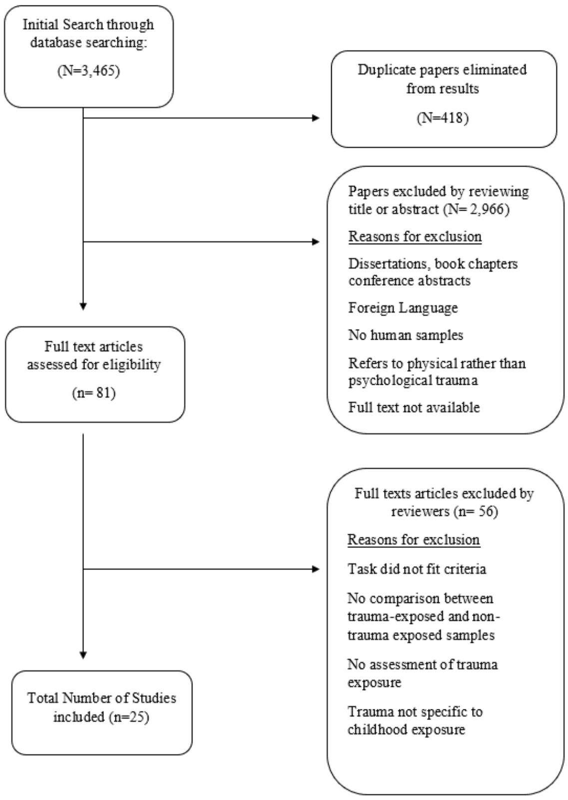


Table 6.1 Summary of included Studies

Study	Country	Sample Source	N	% female	Mean age (SD)	Trauma Type	N(%) exposed	bias	Main Findings
Allen, 2017	USA	General population	4351	NR	33.2 (10.7)	Multiple	1789 (41)	LOC	Exposed: LOC = 30.31 (SD = 3.9) Unexposed: LOC = 30.16 (4.09) Reported as no difference (adjusted for sex)
Andreou, 2000	Greece	School	181	56	10.2 (1.7)	Bullying	34 (18.7)	LOC	Exposed[1]: LOC = 12.13 (SD = 2.41) Unexposed: LOC = 7.23 (SD=1.03)
Asberg., 2014	USA	Prison	39	100	37.82 (8.82)	Sexual Abuse	23 (59)	LOC	Exposed: LOC = 10.79 (SD 3.9) Unexposed: LOC = 8.87 (SD = 3.4) p = 0.15
Atik, 2013	Turkey	School	742	53	13.11 (0.92)	Bullying	158 (21.3)	LOC	Exposed: LOC = 15.01 (SD=4.38) Unexposed: LOC = 12.9 (SD = 4.40)
Barahal, 1981	USA	Social services & Non-exposed from local summer camp	33	31	7.5 (NR)	Multiple	17 (53)	LOC	Exposed LOC= 6 (SD 2.21) Unexposed: LOC = 8.7 (SD 1.62) p=.006 (adjusted for IQ)

Table 6.1 Continued

Beck -Sander, 1997	UK	Outpatient	42	0	NR	Sexual Abuse, Physical Abuse	SA: 22 (52) PA: 21 (50)	LOC	Exposed: LOC = 21.24 (SD = 18.5) Unexposed: LOC = 18.5 (SD = 5.8) Reported as NS (adjusted for age, parental SES, type of maltreatment)
Ireland., 2015	UK	School	198	73	20.18	Sexual Abuse	44 (22.2)	LOC	Exposed = 46.1 (SD = 7.8) Unexposed = 48.2 (SD = 8.5) Analysis reported as NS
Luciano & Savage, 2007	Canada	School	27	48	10.9 (NR)	Bullying	NR	LOC	Correlation = .554 (p<.01) Adjusted for vocabulary and reading ability
Mannarino,1996	USA	Rape crisis centre & matched controls	165	100	10 (NR)	Sexual Abuse	77 (46.7)	LOC; AS	LOC Exposed = 16.6 (SD = 4.7) Unexposed = 15.7 (SD 4.9) t(1,164) = 1.1 NS (Adjusted for ethnicity and SES) AS (bad events) Exposed = 7.4 (SD =2.6) Unexposed = 6.4 (SD=3.1) t(1,164) = 2.2 p<.05
Marsh, 2011	AUS	School	4,082	57	13.8 (1.4)	Bullying	NR	LOC	positive relationship reported between external LOC and bully/victim factor loadings between .08-.26 p<05
McNally 2006	USA	General	174	73	NR	Bullying	138 (79.3)	SM	Sensitivity (d’), adjusted for sex:

Table 6.1 Continued

		Population							Block 1: r=0.12, p= .07; block 2: r=0.19, p= .01) No difference in response bias (criterion)
Moran & Eckenrode, 1992	USA	Social care referrals & school	145	100	NR	Multiple	33 (22.8)	LOC	Mean LOC NR Multiple regression LOC (good events) B=.46, p=.01 AdjR2 = .14 B=.46, p=.01
Moyer, 1997	USA	Social care referrals & school	201	100	NR	Sexual Abuse	43 (21)	LOC	Exposed = 16.7 (SE 0.66) Non-exposed = 12.2 (SE 0.38) p<.001
Muller 1994	USA	University	866	68	18.9	Physical Abuse	323 (36)	LOC	Exposed= 17.29 (SD = 4.9) Not Exposed 16.95 (SD =4.83) Correlation = .21 p<.05 (Adjusted for sex)
Porter & Long, 1999	USA	University	369	100	20 (3.98)	Sexual Abuse	84 (22)	LOC	Trauma = 12.81 (SD = 8.52) Not Exposed 11.28 (SD = 3.71) Reported NR (Adjusted for age)
Radliff, 2016	USA	School	469	57	13.21, (0.97).	Bullying	277 (59)	LOC	Trauma = 14.33 (SD = 5.15) No Trauma 12.15 SD = 4.84) p = .003, Hedge's g = .44, (Adjusted for school, age and grade)
Roazzi, 2016	Italy	Social Services referrals & General	160	37	10.96 (2.9)	Multiple	60 (37.5)	LOC	higher scores in maltreatment group on LOC (M==21.93 vs 18.56 F(1,152)=14.84, p<.001.

Table 6.1 Continued

		Population							(Adjusted for SES).
Rucklidge, 2006	NZ	General Population	114	50	40.5 (12.2) - 44.8 (7.2)	Multiple	64 (57)	AS	Analysis reported as NS (Adjusted for age)
Yamasaki, 2016	Japan	General population	4277	47	9.8 (0.4)	Bullying	522 (12.2)	LOC	4.66 (SD 1.89) Direct path coefficient Bullying - external locus of control .12 (p<.001)

NOTE abbreviations: JTC = ‘Jumping to Conclusions’ Bias PRT = Probabilistic Reasoning Task AS = Attribution Style NR = Not Reported NS = Not Significant [1] LOC measure reverse-scored in analysis (a higher value denotes a less external LOC) * = combined groups: bully/victims and victims of bullying **combined mild and severe bullying. All LOC and AS scores are reported mean values, and a higher LOC signifies a more external LOC and higher AS signifies more external AS.

6.5.2 Meta-Analysis

The meta-analysis had a total of 12,691 participants from the 14 studies that were suitable to be included. The median sample size was 155 participants (range 27 to 4,351). An average of 41.2% (SD = 18.7) of the participants was exposed to trauma. Results for subgroups of trauma exposure were combined in a pooled analysis for three studies (Andreou, 2000; Hovens et al., 2016; Radliff, Wang, & Swearer, 2016). One study (Beck-sander, 1995) reported two results from the same sample (one for exposure to physical abuse and one for exposure to sexual abuse). Only the exposure with the higher prevalence (sexual abuse) was included to reduce bias in the pooled analysis.

The SMD suggested a greater (more external) LOC in the exposed group (SMD Median = 0.40, Inter-quartile range 0.07 to 0.52). However, there was substantial heterogeneity between studies (I^2=92.9%). As illustrated in Figure 2, one study (Andreou, 2000) was a clear outlier in the analysis. When omitting this study, the I^2 value reduced to 81.2%.

Figure 6.2 Meta-Analysis of Association Between Exposure to Childhood Trauma and Locus of Control

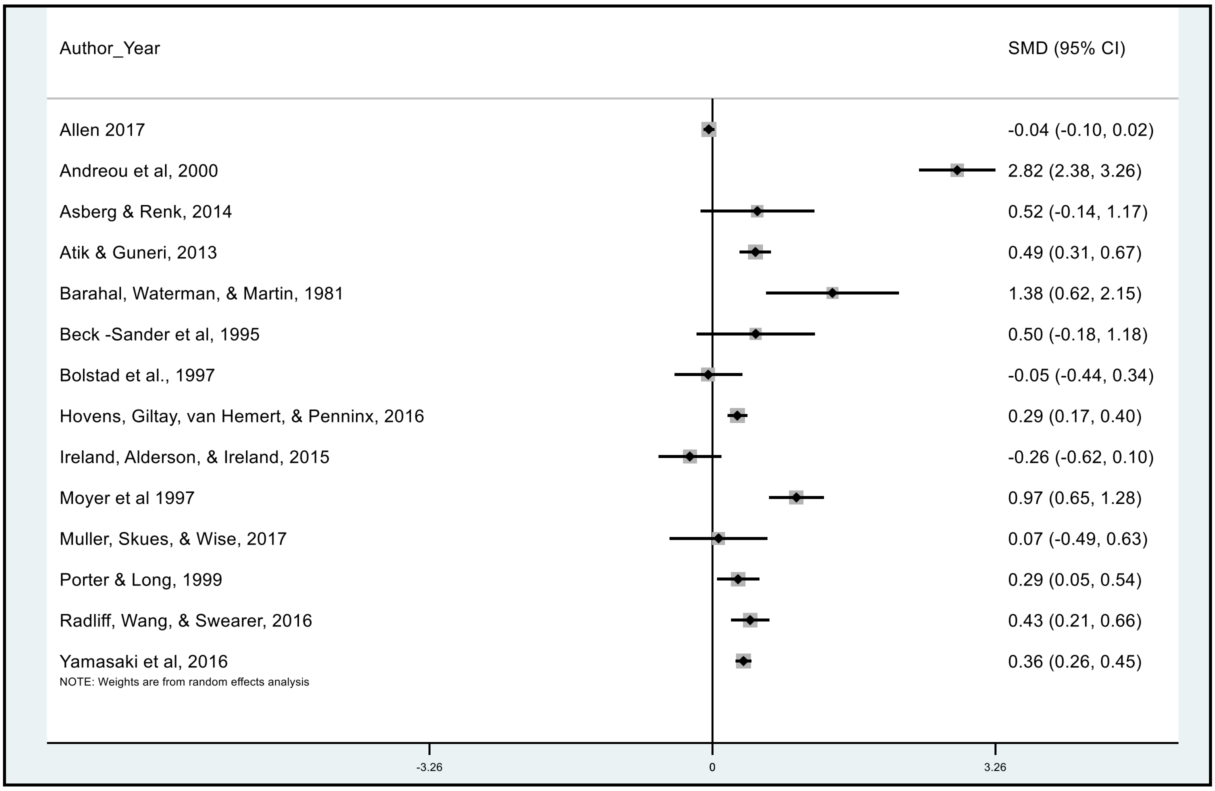


Figure 6.2 Note Abbreviations: SMD – Standardised Mean Differences (95% confidence interval). NOTE: Comparison of difference between mean scores on Locus of Control self-report measures between groups that are exposed or unexposed to childhood trauma. A greater LOC score indicates a more external LOC

6.5.3 Meta-Regression

I carried out a series of meta-regressions to examine possible sources of variation between studies. None of the variables that I examined (study quality, recruitment sample, mean age, and sex distribution of sample) were associated with effect sizes across the included studies. The I^2 value was reduced to the greatest extent by including the sex distribution of the sample (76.3%; see Table 6.2).

Table 6.2 Meta-Regression of pooled analysis[1]

	Coefficient	Confidence Intervals	*p*	I^2 (%)
Mean Age	-.013	-.04, .01	0.241	88.0
% female	-.002	-.012, .001	0.537	76.3
Recruitment sample*	0.50	-.15, .1.15	0.120	90.1
Trauma Type**	.014	-58, .61	0.957	84.4
Quality Assessment score	-.22	-.59, 1.4	0.206	91.4
Use of validated LOC measure***	0.33	-0.62, 1.29	0.459	95.5

Note: [1]All analyses exclude one study (Andreou et al., 2000) identified as an outlier in the main analysis *Population-based or not population-based **Single or multiple trauma types ***Measures of LOC using validated measures (Levenson's, Rotter's, Nowicki Strickland) or other

6.5.4 Narrative Synthesis

6.5.4.1 Locus of Control

Five studies were not included in the meta-analysis due to insufficient data (Fredstrom et al., 2011; Luciano & Savage, 2007; Marsh et al., 2011; Moran & Eckenrode, 1992; Roazzi et al., 2016). There was some evidence of an association between exposure to trauma and an external LOC reported by all five studies. Three studies examined forms of peer victimisation (correlation with a more external LOC ranging from r=.23 to r=.55; p-values <0.05 to 0.003; Fredstrom et al., 2011; Luciano & Savage, 2007; Marsh et al., 2011) and two reported a relationship between maltreatment and a more external LOC (Moran & Eckenrode, 1992; Roazzi et al., 2016).

The included studies varied in the study sample and the type of trauma measured. Fredstrom and colleagues (2011) reported a higher external LOC associated with school-based and electronic bullying; the association between external LOC and electronic bullying remained after adjusting for school-based victimisation in a regression model. Luciano and Savage (2007) reported an association between a more external LOC and victimisation in a sample with and without learning difficulties. Long-term maltreatment was also associated with lower internal LOC for good events when adjusting for the age of onset of maltreatment, depression and level of self-esteem (Moran & Eckenrode, 1992).

6.5.4.2 External Attribution Bias

Two studies examined the association between childhood trauma and external attribution bias. One study (Rucklidge et al., 2016) examined the external attribution bias in participants with and without attention deficit hyperactivity disorder but found no association with childhood trauma in either group. In the other study, sexually abused children reported more external, unstable and specific causal attributions to negative events compared to non-abused children ($p<.05$; Mannarino & Cohen, 1996).

6.5.4.3 Source Monitoring

Three papers examined performance on source monitoring tasks. Two of these did not report any evidence of an association between trauma exposure (62%-79% exposed) and source monitoring: one involved a sample of first-episode psychosis patients (Bendall et al., 2011), and the other involved a sample of female, acute psychiatric patients (Chiu et al., 2016). In the third paper, using a non-clinical sample, participants who reported exposure to sexual abuse had a lower sensitivity (d') in distinguishing between real and imagined stimuli compared to non-exposed individuals (block 1: $r=0.12$, $p= 0.07$; block 2: $r=0.19$, $p= 0.01$) (McNally et al., 2005).

6.5.4.4 Jumping to Conclusions Bias

One study (Freeman et al., 2008) tested for the presence of the JTC bias, and it did so in a sample of 200 members of the general population. Twenty per cent of this sample demonstrated this bias, but there was no association with childhood trauma (OR=1.1, 95% CI

0.44, 2.75; p=.831). The proportion of the sample exposed to childhood trauma was not reported.

6.5.5 Quality Assessment

Table 6.3 provides a summary of the assessment of quality for the included studies. Quality scores ranged from 1 to 5. Six studies (24%) fulfilled over half of the criteria, and the mean score across the 25 studies was 2.72 (SD=1.06). The most poorly met criteria were related to sampling. Twenty-one studies (84%) did not use a random sample or sample a complete group, and 15 studies (60%) either had a low response rate (<75%) or failed to report a response rate. Of the six studies that described sampling from separate groups, two studies (Barahal et al., 1981; Rucklidge et al., 2016) described sampling from the same community and assessed as being representative of the exposed cohort. Of the remaining four studies, two reported a higher SES in the non-exposed group and adjusted for this in the analysis (Mannarino & Cohen, 1996; Moyer, DiPietro, Berkowitz, & Stunkard, 1997), and two did not provide details of whether the groups were from the same community (Bendall et al., 2011; Moyer et al., 1997).

Sixteen (64%) of the studies included in the review described procedures that aimed to minimise observer bias in assessing the outcome, most commonly through delivering self-report measures. Fifteen studies (60%) controlled for at least one variable that was identified by reviewers as a potentially important confounder. Only two studies (8%) adjusted for multiple confounding variables. In these two studies, IQ attenuated the relationship between abuse and LOC in one study (unadjusted p=0.001; adjusted p=0.006; Barahal et al., 1981) and no attenuation was reported when adjusting for sex in the other (Fredstrom et al., 2011).

6.5.6 Assessment of publication bias

The results from the Egger's regression provides weak evidence of an asymmetrical distribution in the funnel-plot of the meta-analysis. The estimated bias coefficient is 3.15 (95% CI = <.001, 7.03, p=0.050; funnel plot Appendix Figure 4.4).

Table 6.3 Quality Assessment of Included Studies

	Random or complete sampling[1]	Response rate 75% or more	Non-exposed representative of exposed	Confounder Adjustment	Observer Bias Minimised	Total score
Allen et al., 2017	Yes	Yes	Yes	Yes*	Yes	5
Andreou, 2000	No	No	Yes	No	Yes	2
Asberg & Renk, 2014	No	No	Yes	No	Yes	2
Atik & Guneri, 2013	No	No	Yes	Yes*	Yes	3
Barahal, 1981	No	No	Yes	Yes*	No	2
Beck -Sander 1997	Yes	Yes	Yes	No	Yes	4
Bendall, 2011	No	Yes	No	No	No	1
Bolstad., 1997	No	No	Yes	No	Yes	2
Chiu et al., 2016	No	Yes	Yes	Yes**	No	4
Fredstrom., 2011	No	Yes	Yes	Yes*	Yes	4
Freeman, 2008	No	No	Yes	No	Yes	2
Hovens, 2016	No	Yes	Yes	Yes*	No	4
Ireland, 2015	No	No	Yes	No	Yes	2
Luciano & Savage, 2007	No	No	Yes	Yes*	No	2
Mannarino, 1996	No	No	No	Yes*	No	1
Mcnally 2006	No	Yes	Yes	Yes*	Yes	4
Marsh., 2011	Yes	No	Yes	No	No	2
Moran., 1992	No	No	No	Yes**	No	2
Moyer, 1997	No	Yes	No	No	No	2
Muller 1994	No	No	Yes	Yes*	Yes	3
Porter & Long, 1999	No	No	Yes	Yes*	Yes	3
Radliff, 2016	No	No	Yes	Yes	Yes	3
Roazzi, 2016	No	No	Yes	Yes*	Yes	2
Rucklidge, 2006	No	-	Yes	Yes*	Yes	3
Yamasaki, 2015	Yes	No	Yes	No	Yes	4

[1]Scored as 1 if 'Yes'; 0 if 'No'

6.6 Discussion

This chapter aimed to provide a review of studies to date that investigated the relationship between trauma and cognitive and perceptual biases associated with psychosis. The results of the study are, due to the proportion of studies that examined each bias included in the search criteria, predominantly from an analysis of the relationship between childhood trauma and LOC. The review highlights key methodological considerations for this area of study and directions for further research.

6.6.1 Main findings from studies of LOC

The results from the pooled analysis, which included 14 of the 19 studies that examined LOC, provided some evidence that exposure to childhood trauma is associated with an increased risk of a more external LOC based on the difference of SMD values between exposed and non-exposed groups in each study. The narrative synthesis of LOC studies that I was unable to include in the meta-analysis report an association between exposure to victimisation and long-term maltreatment.

However, the results of the meta-analysis are highly heterogeneous (I^2 >75%), which inhibits interpretation of the estimated effect size of the association between exposure to childhood trauma and increased risk of external LOC from the pooled analysis. Meta-regression analyses of these results suggest that this heterogeneity is not accounted for by quality rating, demographic variables or study characteristics or whether studies used to validate or non-validated measures of LOC.

Nevertheless, the majority of studies of LOC included the review, both in the meta-analysis and narrative synthesis, report an association between childhood trauma and a more external LOC. As a popular psychometric measure, an external LOC is reported to be associated with a range of negative outcomes in mental health (Frenkel et al., 1995; Ye & Lin, 2015), employment (Cobb-Clark, 2015) and educational attainment (Flouri, 2006). The results from my review may suggest that trauma is associated with an increased likelihood of biased cognition associated with the development of adverse mental health outcomes, including psychosis; however, the possible effects of confounding and bias on observed results limits this inference. Trauma may encourage the development of a more external LOC by undermining a sense of agency and generating feelings of helplessness.

6.6.2 Main findings from studies of other biases included in the review

There were few studies of other information-processing biases related to psychosis included in the review that limits making any inferences about their association with exposure to trauma.

There is limited evidence to suggest that children exposed to sexual abuse may have a greater tendency to attribute the cause of negative events to external forces (Mannarino et al., 1994). However, this finding was not present in children exposed to multiple types of trauma (Rucklidge et al., 2016). Further investigation is needed to examine the potential importance of trauma type in the relationship between trauma and external attribution bias.

Findings relating to source monitoring were also mixed. One study found that those exposed to sexual abuse were more likely to have a reduced ability to discriminate between imagined and real stimuli (reality monitoring). However, the remaining two studies did not detect a relationship between trauma and performance on source monitoring tasks.

There is no evidence of an association between trauma and the JTC bias, but this was based on one study with a small number of participants exhibiting the bias (n=40 from a total sample of 200). Therefore, the statistical power to observe an association is likely to have been low (the proportion of the sample exposed to trauma was not reported).

No studies included in the review examined a bias for relying on top-down knowledge to disambiguate new information or a bias against disconfirmatory evidence.

6.6.3 Quality Assessment

The quality assessment of studies highlighted potential sources of bias in a large proportion of the studies: only eight of the studies included (32%) satisfied more than half of the quality assessment criteria. A small proportion of studies (n=8; 32%) reported a response rate of 75% or more and fewer studies (n=4; 16%) reported random or complete sampling. These findings raise the likelihood that results from this review are influenced by selection bias. For example, researchers may recruit participants based on prior knowledge of their trauma exposure or their LOC; a source of potential bias that would not arise if studies used random or complete sampling.

I also considered the role of confounding variables in the quality assessment. Fifteen (60%) of the studies adjusted for confounders in their analysis, but only one study (Barahal et al., 1981) provided information on both unadjusted and adjusted results, meaning the extent to which confounding explains the association between childhood trauma and cognitive biases remains unclear. Based on these findings, the confidence that the associations described in the study are causal is low. It is plausible that other characteristics explain the association between trauma and an external LOC. Factors including lower socioeconomic status, poorer cognitive functioning and family history of mental health difficulties have the potential to contribute to an increased feeling of helplessness and lack of agency that is indexed by external LOC. Therefore, studies must investigate the extent to which these sources of confounding contribute to the observed association between trauma and LOC to infer the true effect of trauma on LOC.

These findings highlight the need for clearer reporting of data for reviews in this area and improvements in methodology in recruitment and increasing participation rates.

6.6.4 Additional findings from reviewed studies

During the review process, I identified studies reviewed in the full-text search that met some of the criteria that may contribute to the discussion of evidence relating to trauma psychosis-related biases (Gawęda, Prochwicz, et al., 2018; Rhodes et al., 1993; Thurber, 1977; Walsh et al., 2007). In studies of adult trauma, the relationship between trauma exposure and a more external LOC was reported. In a study using a measure of trauma and a battery of tests for biases associated with psychosis, external attribution bias was associated with trauma, and there was little evidence of an association with the JTC bias or BADE.

6.6.5 Methodological Considerations

In considering the methodology of the review, the review benefits from several strengths. An established theoretical framework informed the study questions for the systematic review of the trauma to psychosis pathway, which enabled me to have concise research questions and study aims.

The meta-analysis included a large number of participants, and I was able to standardise the measure of LOC from a range of self-report measures. The use of a random-effects meta-analysis and further meta-regression provided avenues to investigate the relationship between trauma and an external LOC. The narrative synthesis of the LOC was consistent with the findings of the pooled analysis, and the review of other biases associated with psychosis gave some insight into an existing evidence base and critical gaps in the current literature. The limitations of the review are discussed in the following sections.

6.6.5.1 Search Criteria

While I endeavoured to include all relevant studies in my search, the search criteria may have led to the omission of key papers by restricting inclusion to peer-reviewed and English-language studies.

6.6.5.2 Data limitations

The availability of data that I required for each study, both for the meta-analysis and the narrative synthesis, limited the study's findings. In the meta-analysis, I was unable to include five eligible studies as authors did not report or provide the necessary data for the pooled analysis on request. Inclusion of these additional studies in the pooled analysis may have substantially altered the results of the pooled analysis. The small number of studies included in the meta-analysis (n=14) also limited the statistical power of the meta-regression and limited carrying out further, more detailed analysis of possible characteristics that may have contributed to the heterogeneity of findings.

For the narrative synthesis, few studies reported results for analysis that did and did not adjust for potential confounders. The lack of reporting of unadjusted and adjusted effects limited the insight the review had into the extent of attenuation of the relationship between childhood trauma and the biases of interest by potential confounders.

6.6.5.3 Variation in the measurement of trauma exposure

The range of trauma types that were assessed, described in Table 6.1, range from single types of trauma, such as bullying and sexual abuse, to multiple types of interpersonal violence. As outlined in Table 6.2, there was a range of methods used to assess exposure to trauma. These methods included referrals from social services and various self-report measures, some of which were developed by study authors and did not provide evidence of validation. Variation in trauma measurement may have contributed to the wide range of exposure prevalence and the variation in results across these studies. The small number of studies identified limited a more in-depth analysis of the role of trauma type with the biases of interest.

6.6.6 Future Directions

The results of this review identify a potential mechanism, namely a more external LOC, associated with exposure to trauma that is also associated with a greater risk of psychosis-related outcomes. While these results have a high level of heterogeneity, it does support further investigation of this relationship. As an external LOC is a bias that can be characterised as a general vulnerability to negative mental health outcomes, it raises the question as to what specific role external LOC has in the pathway to psychosis for individuals who are exposed to trauma and experience symptoms of psychosis.

The role of causality in the relationship between trauma and LOC is one which the review was unable to examine as all studies in the review were cross-sectional. An important question to address in the area is whether trauma precedes a more external LOC to eliminate the possibility of reverse causation. Identifying the temporal relationship between trauma and LOC and whether LOC mediates the trauma to PEs pathway would help to inform interventions that aim to mitigate the effects of trauma on subsequent mental health outcomes.

In consideration of the other biases included in the review, the results highlight a key gap in the literature around cognitive and perceptual biases that may be more strongly associated with psychosis than other mental health outcomes. The bias for the attribution of negative events to external forces may be a bias related to the LOC and, potentially, be specifically associated with psychotic symptoms.

Biases included in the study that are studied predominantly in psychosis literature (the JTC bias, BADE, source monitoring and top-down processing) require further investigation in relation to trauma to identify their theorised pathway from trauma to psychotic symptoms.

I did not include studies that examined the relationship between trauma and biased emotion recognition, a potential mechanism on the pathway between trauma and psychosis, because it had been previously reviewed by da Silva Ferreira and colleagues (2014). Their review of case-control studies (children identified as exposed to abuse from social services referrals compared to controls), reported mixed findings regarding the relationship between trauma and emotion recognition biases. The conclusions that can be drawn from the review are limited by the small number of included studies (n=17), variation in tasks used and the different emotion recognition-related outcomes (ability to recognise emotions, identification of emotional intensity, bias for attributing hostility to neutral stimuli) that were assessed. In a study subsequent to da Silva Ferreira and colleagues' review, there was little evidence of a relationship between exposure to trauma and emotion recognition deficits at age 8 years using a large sample from the ALSPAC cohort (Dunn, Crawford, et al., 2018).

Da Silva Ferreira and colleagues' (2014) review did report that some studies found evidence to suggest that trauma-exposed children were more likely to identify angry emotions in neutral situations more frequently (hostile attribution bias) compared to controls. As there is evidence of an association between hostile attribution bias and symptoms of psychosis (Buck et al., 2020; Mancuso et al., 2011; Park et al., 2018), further investigation of hostile attribution bias as a candidate mediator on the pathway from trauma to psychosis-related outcomes may be warranted.

6.7 Conclusion

In this chapter, I presented a systematic review and meta-analysis of the current literature of studies of trauma and cognitive and perceptual biases associated with psychotic symptoms. The evidence lends support to the relationship between exposure to childhood trauma and a more external LOC; however, this was highly heterogeneous. The heterogeneity detected in the pooled analysis was not explained by demographic variation or differences in study characteristics, including study quality. As an external LOC is associated with a wide range of negative mental health outcomes, this review is limited in the conclusions that can be drawn regarding the relationship between trauma and cognitive and perceptual biases that are specifically associated with psychosis. The review does suggest that an external LOC may be a mechanism for how trauma increases the risk of a range of negative mental health outcomes. As the review is based on cross-sectional evidence, no conclusions can be made about the direction of causality in the association between childhood trauma and the likelihood of external LOC reported in the study.

The small number of studies of other biases included in the review provided mixed evidence for a relationship between childhood trauma and external attribution bias, source monitoring and insufficient evidence to infer any relationship with the JTC bias. The review also concludes that there is a paucity of studies investigating trauma and BADE and the top-down processing bias.

Chapter 7 Study III: The relationship between childhood trauma, abnormal belief-updating, and psychotic experiences

7.1 Background

7.1.1 The ‘Jumping to conclusions’ bias

As discussed in Chapter 2, previous studies have found that there is an association between information-processing biases and an increased risk of psychosis-related outcomes. Several studies have examined information-processing biases using a probabilistic inference task (the beads task) to infer whether individuals have a bias towards making decisions hastily, which is referred to as the ‘Jumping to conclusions’ (JTC) bias. Previous studies have characterised the JTC bias as an indicator of increased vulnerability to adopting delusional beliefs and is targeted in meta-cognitive interventions for psychotic symptoms (Dudley, Taylor, Wickham, & Hutton, 2015; Freeman & Garety, 2014, Ishikawa et al., 2019; So et al., 2015).

As discussed in chapter 2, evidence for the association between the JTC bias and PLEs in general population samples is weaker and less consistent than that with psychotic disorder in clinical samples (Dudley et al., 2015; So, Siu, Wong, Chan, & Garety, 2016; Colbert & Peters, 2002; Freeman, Pugh, & Garety, 2008; Gawęda et al., 2018; Tripoli et al., 2020; So et al., 2016). The differences in findings may be due to the differences in study designs between general population and clinical samples (i.e. case-control and cross-sectional studies) that may lead to bias and confounding in observed results. Some studies have not found evidence of an association between the JTC bias and PLEs (Ross et al., 2016; So and Kwok, 2015; Ward et al., 2018). Recent studies have provided mixed evidence of an association between the JTC bias and PLEs in large general population samples (Reininghaus et al., 2018; Ross et al., 2016; So and Kwok, 2015; Ward et al., 2018), which makes the strength of the association between the JTC bias and PEs unclear and warrants further investigation in a general population sample.

7.1.2 What accounts for the ‘Jumping to Conclusions’ bias?

Studies have taken several approaches to understand what latent belief-updating processes contribute to the JTC bias (e.g. the calculation of odds, prior expectations, confidence in estimations, motivation, affect, learning rate, salience attribution; Stuke et al., 2017). These approaches include the use of modified versions of the beads task and the application of computational modelling to behavioural data to infer specific belief-updating processes.

In a modified version of the beads task (the probability estimation task; Chapter 2), participants with psychotic symptoms tend to revise estimations more dramatically in response to contrary information compared to controls when completing the task; this tendency is referred to as an ‘over-adjustment’ bias (Colbert and Peters 2002; Fear and Healy 1997; Garety et al. 1991; Jardri et al. 2017; Peters and Garety 2006; Rodier et al. 2011; Speechley et al. 2010)**.** As with the JTC bias, there are limitations to this evidence and, to my knowledge, no previous study has analysed performance on the probability estimation tasks and PEs in a large general population sample.

Recent studies have used computational modelling to analyse performance on versions of the beads task to infer what specific belief-updating processes are associated with psychosis-related outcomes (Adams et al., 2018; Ermakova et al., 2017; Moutoussis et al., 2011; Stuke et al., 2017). These studies provide limited evidence of an association between specific belief-updating processes and a greater likelihood of psychotic symptoms in clinical populations. Furthermore, these studies have not examined the potential role of confounding in this relationship or tested these models using data from a large general population sample. Investigating the association between belief-updating processes and PEs in a general population sample may have implications for studies of psychotic disorders by testing the role of confounding more thoroughly than case-control studies in clinical samples.

It is also unclear whether these abnormal belief-updating processes increase the likelihood of the risk of PEs more broadly or only specific types of psychotic symptoms, i.e., hallucinations or delusions. Furthermore, the relationship between abnormal belief-updating processes and non-psychotic psychopathology has not been investigated. Therefore, it is unclear whether abnormal belief-updating is specifically associated with psychotic outcomes or an increased vulnerability to psychopathology.

7.1.3 The role of belief-updating on the pathway from trauma to psychotic experiences

As discussed in previous chapters, understanding the potentially causal relationship between trauma and PEs would inform models of psychosis and may inform interventions that aim to mitigate the risk of PEs for those exposed to trauma. It is currently unclear whether exposure to trauma does increase the likelihood of abnormal belief-updating processes associated with psychosis-related outcomes. Understanding whether trauma causes abnormal belief-updating and, in turn, increases the risk of PEs, would inform integrated models of psychosis and may identify potentially modifiable processes on the pathway from trauma to PEs.

7.2 Aims of the chapter

This chapter aims to address the following questions:

1. Is there an association between abnormal belief-updating processes and an increased likelihood of psychotic experiences at age 24 years?
2. Is the association between abnormal belief-updating processes and psychotic experiences specific to hallucinations or delusions?
3. Is there an association between abnormal belief-updating processes and an increased likelihood of non-psychotic psychopathology (depression or anxiety)?
4. Is there an association between exposure to trauma and an increased likelihood of abnormal belief-updating processes?
5. To what extent are these relationships attenuated by confounding?
6. Do abnormal belief-updating processes mediate the relationship between exposure to trauma and the risk of psychotic experiences?

7.3 Methods

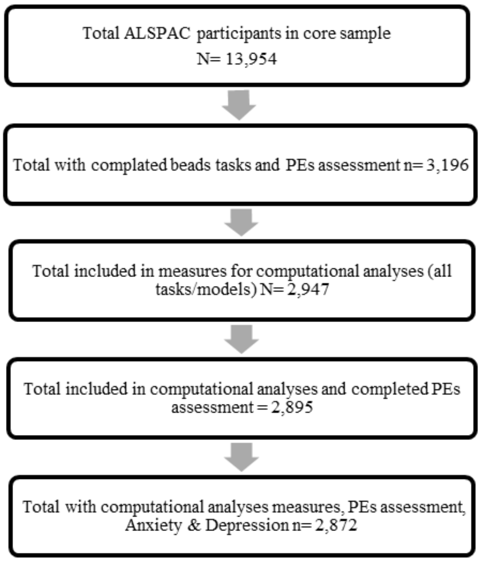
7.3.1 Sample

A total of 3,196 participants completed the beads tasks and PEs assessment at age 24 years. Of these, 2,872 were included in the main analyses based on data availability and model fit (see Figure 7.1).

7.3.2 Measures

Measures used in this chapter are briefly summarised below. Further details for each measure can be found in the methods Chapter 5.

Figure 7.1 Flow Chart of Study III participant inclusion



7.3.2.1 Mental health measures

The mental health main outcome in this chapter is psychotic experiences. I used measures of symptoms of psychosis (hallucinations, delusions) and non-psychotic psychopathology (depression, anxiety) to investigate research questions relating to potential symptom specificity.

Psychotic experiences

Psychotic experiences were assessed at approximately age 24 years using the Psychosis-like Symptoms semi-structured interview (PLIKSi), which was carried out by trained psychologists. The interview assesses the presence of 13 psychotic experiences (12 items also assessed at age 18 years listed in Chapter 4 and, additionally, tactile hallucinations) including hallucinations, delusions and thought interference.

The main outcome used in study III was distressing or frequent PEs in the last 12 months. For sensitivity analyses, I examined a broader outcome of PEs (any reported past-year suspected or definite PEs) and a narrower outcome of psychotic disorder, which is defined as the presence of PEs that had occurred at least once per month in the last six months and led to help-seeking, poorer social or occupational function, or was very distressing (Zammit et al., 2013).

To examine symptom-specificity of the association between abnormal belief-updating processes and PEs, I also examined, as outcomes, the presence of past-year frequent or distressing hallucinations and past-year frequent or distressing delusions.

Anxiety and depression

Anxiety disorder and depressive disorder were assessed at approximately age 24 years using the clinical interview schedule revised (CIS-R) based on ICD-10 criteria. The outcomes analysed were depressive disorder (either moderate or severe) and anxiety disorder, which included generalised anxiety disorder, panic disorder, social phobia, and specific phobias (Brugha et al. 1999).

<u>7.3.2.2 Belief-updating tasks</u>

I used two different versions of the beads task to assess processes relating to belief-updating. The first version of the beads task, here referred to as the Draws to Decision (DTD) task, has been used in a large number of previous publications (for discussion see Chapter 3). This task examines how quickly individuals reach a decision when given a limited amount of information (Dudley et al., 2015; Fine, Gardner, Craigie, & Gold, 2007). The second version of the beads task, the probability estimation task, examines how participants update their probability estimations in response to new information (Fear & Healy, 1997). The procedures for each task are detailed in Figure 7.2. Both tasks were carried out when participants were approximately 24 years of age.

Participants completed the tasks at the ALSPAC clinic, where computerised versions of the tasks were presented using Matlab.

Figure 7.2 Outline of task procedures for belief-updating tasks

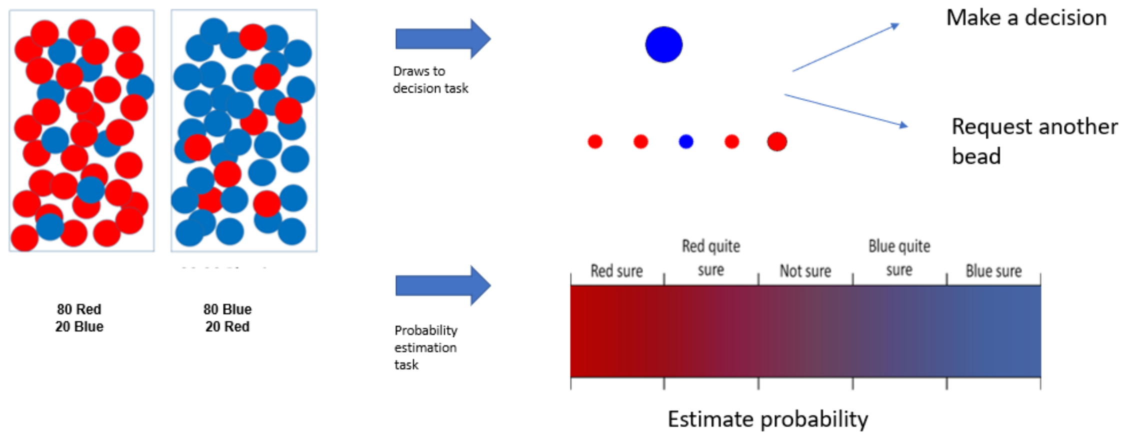


Figure 7.2 Note: Participants were presented with an illustration of two jars with two different colours of beads and told that they contain 100 beads with inverse proportions of coloured beads at a ratio of 80:20 (left). They were then told that the computer would randomly choose a bead from one of the jars, show it to them, and then put it back in the jar. In the draws to decision version of the task (top right), the participant could either state which jar the bead was drawn from after the first bead or request to see another bead, which was drawn from the same jar. Participants could request up to ten beads before deciding from which jar the beads were being drawn. The number of beads that were requested is referred to as ‘draws’. This task was completed five times with five different sequences of beads, and the participants were told that the computer selects the jar at random each time. In the probability estimation task (bottom right) The participants were told that they would be shown a sequence of 30 beads. Every time a bead was presented, the participant had to rate how certain they were about from which jar that the beads were being drawn. Every participant was shown the entire sequence of 30 beads. They were also told that the jar that the beads were being drawn may or may not change during the task at any point in the sequence and may change multiple times.

7.3.2.2.1 Draws to Decision task

The draws to decision task used an 80:20 ratio of beads over a series of five blocks (i.e. completed the task five times). Participants could request up to ten beads before deciding from which jar the beads are drawn. The average draws to decision (DTD; the number of beads presented from a fixed sequence before a participant decides from which jar the beads are drawn) from the performance of the five blocks was recorded. In order to compare my findings to previous literature, I used two behavioural indices from the task in my analyses: mean DTD and the JTC bias (an average DTD of two beads or less). The limitations of these behavioural indices will be discussed later in the chapter.

In addition to DTD and the JTC bias, two computational indices were derived from performance on the task by Dr Michael Moutoussis using a ‘costed Bayesian model’, described in previous studies (Ermakova et al., 2017; Moutoussis et al., 2011). This model approximates how close the participants’ performance is to optimal during the task. The model derives values of (i) the posterior probability that the beads are drawn from each jar at each point of the sequence based on the colours of beads presented and (ii) the value of different decisions (action value) made. Two indices are derived using these values as measures of belief-updating processes that drive performance on the task: cost of sampling and decision noise.

Cost of sampling

As the value (i.e. penalty or reward) for drawing additional beads is not stated, the cost of sampling indices estimates the subjective value that participants attribute to requesting additional beads. A high cost of sampling could account for the JTC bias by demonstrating that there is a consistent strategy where a greater cost is the basis for requesting less information before deciding. A higher perceived cost of sampling would indicate a greater desire to complete the task, which may be due to motivational factors including intolerance of uncertainty or a possible perceived cost to self-esteem when requesting further information (Ermakova et al., 2017; Moutoussis et al., 2011). The cost of sampling index was not normally distributed and difficult to transform; therefore, I derived a dichotomous variable which grouped the top 10% of participants versus the bottom 90% (Figure 7.3).

Decision noise

A high decision noise value would suggest participants are either inconsistent in their performance across the five blocks or that they are using a non-standard strategy that is not indexed by the model to complete the task. This parameter was also not normally distributed and difficult to transform; therefore, I grouped the top 10% of participants versus the bottom 90%.

7.3.2.2.2 Probability estimation task

This task also presents participants with two jars of 80:20 ratios of coloured beads. Participants were required to rate the probability, on a sliding scale, that each bead in a sequence of 30 beads was being drawn from one jar or the other in a single block. The jar the beads were drawn were switched (e.g. from mainly red to mainly blue) after 15 beads. Participants were told the jars may switch at any time, but not how many times the jars will switch, if at all, or at what point in the sequence. The same sequence of beads was presented to all participants. A behavioural measure of ‘contrary updating’ was derived, based on previous studies of the task (Adams et al., 2018; Peters & Garety, 2006) which is the absolute value of the mean change in estimation after seeing a bead of a different colour to at least two same-colour previous beads (e.g. the percentage change in estimation when seeing a blue bead after seeing two or more red beads).

For computational modelling of the probability estimation task, Dr Rick Adams tested four potential models and selected a model based on the best fit to data using Bayesian model selection. The most suitable model to fit the dataset was the Hidden Markov Model (HMM; FitzGerald, Hämmerer, Friston, Li, & Dolan, 2017). The HMM model generated five indices that are each measures of latent characteristics of belief-updating: the expectation of reversal, adjustment rate, inference length, estimation confidence, and decision noise (detailed below).

Expectation of reversal

Based on participants' responses over the beads sequence, the model estimates the participants' prior expectation that the jar will switch during the beads sequence, indexed by the expectation of reversal parameter. A high expectation of reversal would suggest participants revise their beliefs to a greater extent when presented with a bead of a contradictory colour to previous beads in the sequence. Based on previous literature, I hypothesised that a greater expectation of reversal would be associated with PEs. There was an absence of previous studies that have examined the relationship between the expectation of reversal and exposure to trauma or other mental health outcomes. As the parameter was not normally distributed and difficult to transform, I grouped the top 10% of the participants versus the bottom 90%.

Adjustment rate

Over the sequence of beads, participants may differ in how much new information affects their latest probability estimates of from which jar the beads are drawn. A higher adjustment rate would suggest that participants are quick to adjust their estimates in response to new information. This measure was transformed on a logarithm scale and analysed as a continuous measure.

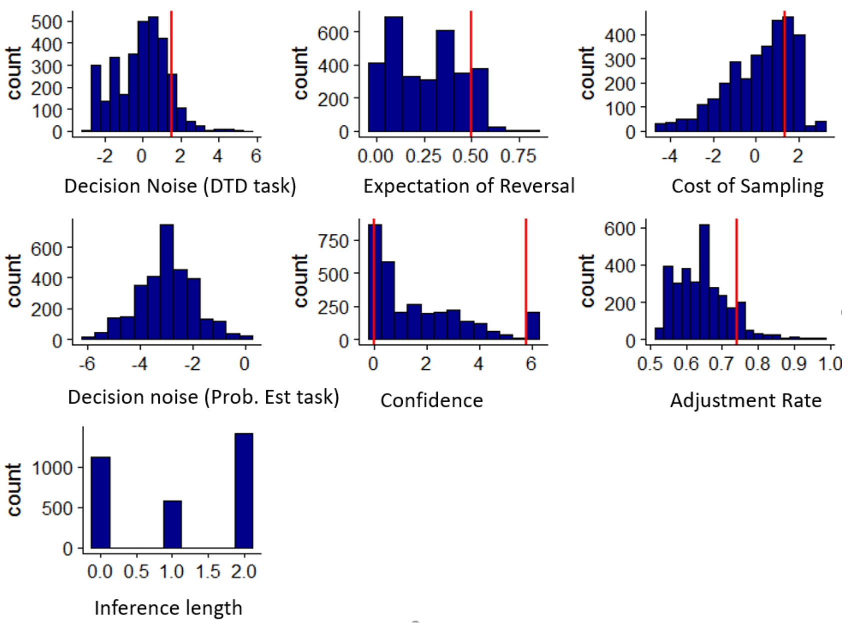
Inference window

Participants may differ in how many of the previously presented beads they use to inform their current bead probability estimate (e.g. is it the colour of the most recent bead or the colour of the previous three beads that is informing a current estimate?). Differences in inference window may contribute to abnormal belief-updating associated with PEs. The inference length parameter estimates the approximate number of previous beads that participants consider when making a current estimate. This measure was divided into categories of 0 previous beads used, 1-2 beads and 2-4 beads used.

Estimation confidence

The model also estimates how confident participants are in their prior estimations. A lower confidence value would suggest that participants are more willing to revise their prior beliefs in response to new information compared to those with higher confidence. Findings relating to decision confidence in belief-updating in psychosis literature are inconsistent (i.e. whether higher or lower confidence is associated with psychosis-related outcomes). Therefore, I analysed both high confidence and low confidence as two categories of interest from a single parameter (i.e. a three-category variable with a middle category as baseline).

Figure 7.3 Distribution of belief-updating indices and derivation of categorical and binary measures



Note: Red lines denote partition of data for categorical or binary measures

Decision noise

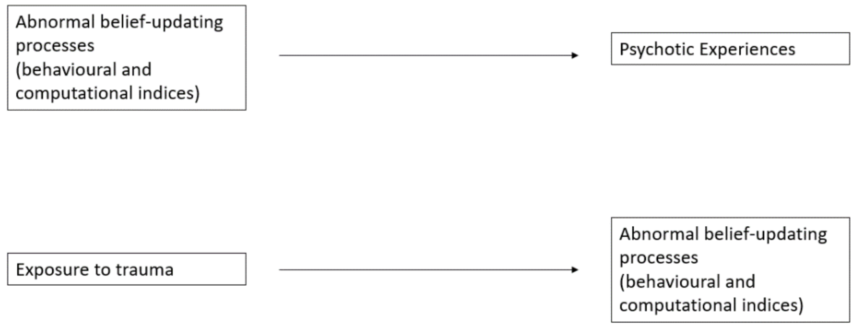
Lastly, the model estimates a decision noise parameter that indexes the extent to which the participants' responses are inconsistent with any of the strategies estimated by the indices described. As with the decision noise parameter in the DTD task, a higher value suggests that participants are using an unmodelled or inconsistent belief-updating strategy. This measure was transformed on a logarithm scale and analysed as a continuous variable.

7.3.2.3 Childhood trauma

As detailed in Chapter 5, I used a measure of trauma exposure based on responses from both parents and children relating to exposure to interpersonal violence and neglect (physical abuse, emotional abuse, emotional neglect, bullying, sexual abuse) between the ages of 0-17 years. As with study I, I used a measure of the number of types of trauma exposure reported (0, 1, 2, 3+) to index an increasing 'dose' of trauma exposure. I examined whether results were consistent with a dose-response effect by using likelihood-ratio tests to compare models using linear terms or categorical terms for trauma exposure. Results from likelihood-ratio testing are consistent with a linear assumption for all models.

I tested each of the indices described for the probabilistic estimation tasks (DTD task and probability estimation task) as potential markers of abnormal belief-updating processes associated with (i) psychotic experiences and (ii) exposure to childhood trauma (Figure 7.4).

Figure 7.4 Directed Acyclic Graphs (DAGs) of analysis of abnormal belief-updating processes in relation to exposure to trauma and psychotic experiences



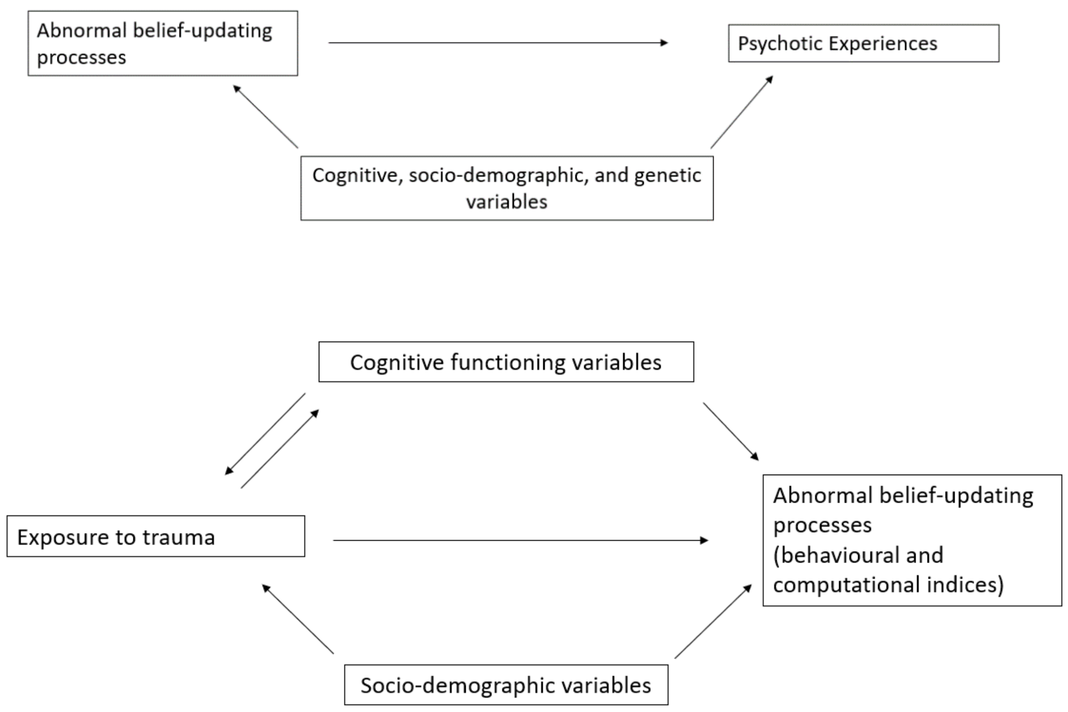
7.3.2.4 Confounders

Based on previous literature and data availability, I included the following measures as potential confounders (see Chapter 5).

Cognitive functioning: Executive functioning, working memory and IQ all assessed at age eight years.
Socioeconomic status: Maternal education, average household income and social class
Genetic risk for schizophrenia: indexed by a polygenic risk score derived using results of the second Psychiatric Genomics Consortium Schizophrenia genome-wide association study.

For the analysis of abnormal belief-updating and PEs, I adjusted for exposure to trauma as a potential confounder. For the analysis of exposure to trauma and abnormal belief-updating, it was unclear whether cognitive functioning is more likely to be a confounder or mediator; therefore, I adjusted for sex and socio-economic measures as potential confounders and adjusted for cognitive functioning separately (Figure 7.5).

Figure 7.5 DAGs of abnormal belief-updating processes in relation to exposure to trauma and psychotic experiences with confounders



7.3.3 Statistical analyses

I completed data analysis in STATA version 15.2 (StataCorp LLC).

7.3.3.1 Preliminary analysis

To inform the main results and ensure that collinearity did not potentially bias my regression modelling, I carried out a correlation analysis of the behavioural and computational variables of belief-updating processes. According to the variable type, I used tetrachoric (binary), polychoric (categorical) and point-biserial (binary and continuous) correlation analyses. There are few prior studies of the relationship between the belief-updating measures and confounding variables studied in this chapter. Therefore, in order to inform current literature, I used regression analyses to test the relationship between each confounder and the likelihood of abnormal belief-updating to inform future studies and the interpretation of my results.

7.3.3.2 Main analysis

7.3.3.2.1 Abnormal belief-updating processes as an exposure

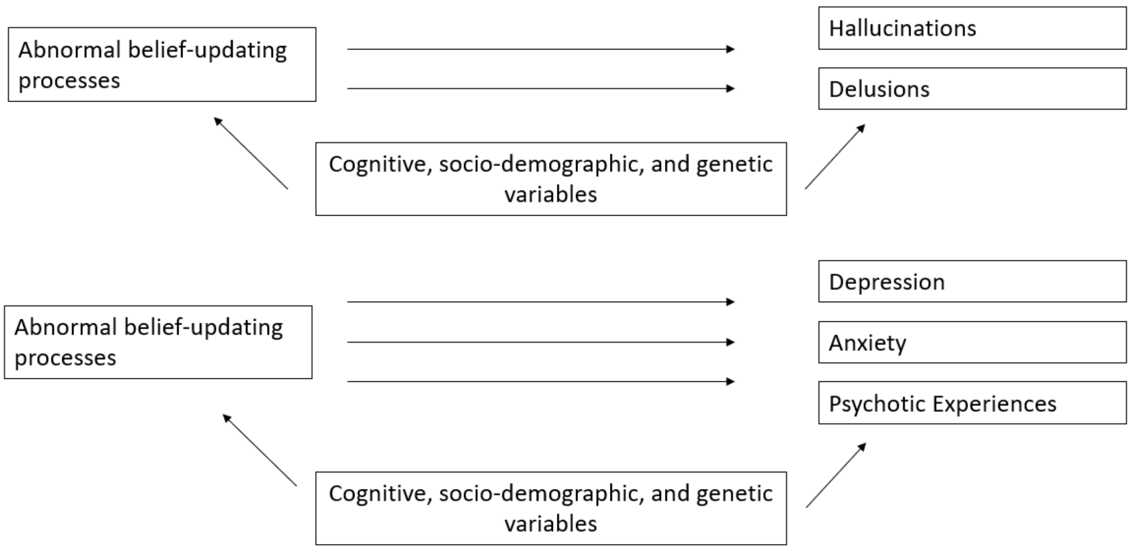
I used logistic regression to analyse the relationship between belief-updating indices and mental health outcomes as the latter were all binary. Belief-updating indices that were categorical variables (inference window, estimation confidence) were entered into the model as indicator variables. In each of the analysis, I derived 95% confidence intervals and Wald test 2-sided *P* values before and after adjusting for confounding.

For analyses of belief-updating processes and symptom specificity, I used bivariate and multivariate probit modelling to model multiple mental health outcomes in a single model. Probit estimates were converted into an approximate odds ratio by exponentiating probit estimates and multiplying them by a factor of 1.6 to aid interpretability (Sullivan et al., 2017). I derived 95% confidence intervals and Wald test 2-sided *P* values for each estimate; a Wald test p-value was used as an index of the strength of evidence that effect size estimates differed between outcomes. I used bivariate probit modelling to model hallucinations and delusions as joint outcomes and multivariate probit modelling to model depression, anxiety and PEs in a single model (Figure 7.6).

7.3.3.2.2 Exposure to trauma and abnormal belief-updating indices

Depending on the parameter distributions, I used logistic or linear regression to test the relationship between exposure to trauma and belief-updating parameters. I tested whether the results were consistent with a linear relationship between the number of trauma exposures and belief-updating parameters by comparing models that treated trauma exposure as an indicator and continuous variables using likelihood-ratio testing. Following this, I used regression analyses to test each parameter as a possible outcome associated with exposure to trauma. I derived 95% confidence intervals and Wald test 2-sided *P* values before and after adjusting for confounding.

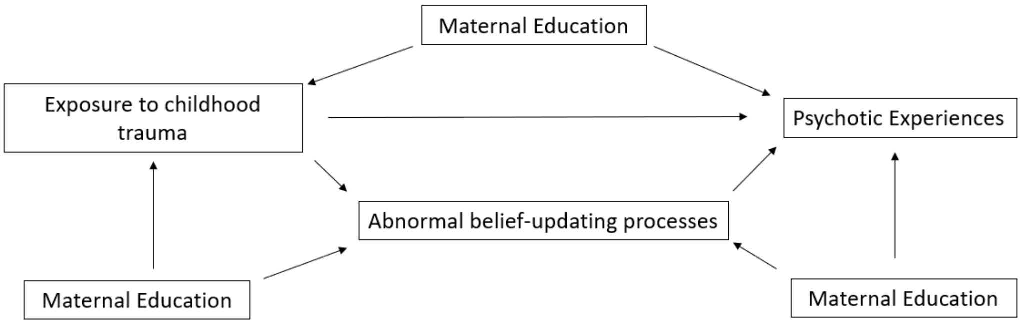
Figure 7.6 DAGs of Study III biprobit and multivariable probit models



7.3.3.2.3 Mediation analyses

Belief-updating parameters that had evidence to suggest that they were associated with both exposure to trauma and PEs were analysed as potential mediators in a mediation model (Figure 7.7). Maternal education was included as a confounder on each of the paths of the mediation analyses. To simplify the mediation model, I used a dichotomous measure of polyvictimisation (exposure to 3+ types of trauma versus exposure to 0-2 types of trauma between 0-17 years of age) as the exposure. Mediation analyses were carried out using the 'paramed' command. Estimates for imputed data were combined for a single effect estimate based on Rubin's rules.

Figure 7.7 DAG of Study III mediation model



<u>7.3.3.3 Sensitivity analyses</u>

To test the robustness of the relationship between belief-updating parameters and PEs, I repeated the main analysis with both a broader measure of PEs (either suspected or definite PEs) and narrower measure of PEs (psychotic disorder) at age 24 years.

<u>7.3.3.4 Handling missing data</u>

The complete sample based on data availability for belief-updating parameters and mental health outcomes was 2,872 (Figure 7.1). A total of 1,562 participants had complete data for exposure to trauma, confounders, mental health measures and belief-updating parameters. To address possible bias from attrition and to have the largest possible sample size, I used multiple imputation to predict values for missing data for exposure to trauma and confounding variables. This method is detailed in Chapter 5.. Analyses using imputed data are reported in this chapter and complete-case data in the appendices (Appendix Tables 5.2 & 5.3).

7.4 Results

7.4.1 Participants

The average age of the 2,872 participants was 24.48 years old (SD 0.8). Those included in the analytic sample were more likely to be female and have higher cognitive functioning compared to ALSPAC participants not included in the sample. The sample was also less likely to have a lower socioeconomic position and an increased genetic risk of schizophrenia (Table 7.1).

7.4.2 Psychotic experiences, depression and anxiety

In the analytic sample, 108 participants were rated as having frequent or distressing PEs in the last 12 months (3.8%). For the broader measure of PEs, 174 participants (6.1%) were rated as having definite or suspected PEs in the last year. A total of 55 (1.92%) participants had psychotic symptoms, and 49 participants (1.7%) had frequent or distressing delusions in the last six months, and 69 (2.4%) had frequent or distressing hallucinations in the last six months. At age 24 years, 204 participants (9.3%) had a moderate or severe depressive disorder and 267 (7.1%) had an anxiety disorder.

Table 7.1 Sample characteristics of participants included in the analytic sample[1]

Reference Category	Analytic Sample Available (n; column %)[2]				
	Included in sample (n=2,872) (n; %)	Excluded from Sample (n=11,804) (n; %)	Odds Ratio	95% CI	P-Value
Female Sex	1,801 (62.7)	5,037 (44.6)	2.09	1.92,2.27	<.001
Lowest Income (bottom quintile)	334 (13.0)	1,739 (23.4)	0.49	0.43,0.56	<.001
Maternal education (<O-level)	471 (16.9)	3,252 (33.9)	0.40	0.36,0.44	<.001
IQ at 8 years old (top quintile)	569 (23.7)	656 (14.2)	1.87	1.65,2.12	<.001
Parental mental health problems	457 (16.0)	1,941 (18.9)	0.82	0.73,0.92	<.001
Exposure to childhood trauma	1,667 (59.8)	4,482 (62.1)	0.91	0.83,0.99	0.04
Genetic risk for SCZ (top quintile)	386 (18.3)	1,166 (20.7)	0.86	0.76,0.98	0.02

Note: [1]Based on complete-case sample [2]The denominators vary for each measure as the number for the participants not included in the analytic sample did not include missing data

7.4.3 Exposure to trauma

A large proportion of the sample (65.8%) reported exposure to trauma, and 23.8% of the sample were poly-victimised (exposed to three or more different types of trauma) between 0-17 years of age.

7.4.4 Performance on belief-updating tasks

For the DTD task, the average number of beads requested before deciding which jar the beads were drawn from was 4.84 (SD= 1.64) and increased over the five blocks (Beta = 0.08; 95% CI 0.07, 0.08; p=<.001). A total of 161 (4.6%) participants made decisions based on an average of two or fewer beads during the five blocks in the task, which is an index of the JTC bias.

For the probability estimation task, mean certainty was lower in the second half (0 = red jar, 1 = blue jar; second half beads 16-30, after swapping jars: mean certainty =0.73, SD=1.89) than the first half (beads 0-15; first half mean certainty= 0.84 SD=1.45). The mean change (based on absolute values) in estimation on seeing a bead of a different colour to the ≥two beads preceding it (contrary updating) in the sample was 0.16 (SD = 1.6).

7.4.4.1 Correlation between indices of belief-updating processes

After transformation of variables, correlations between variables were not high enough to suggest collinearity (see Appendix Table 5.1). There was evidence to suggest that average DTD is negatively correlated with a higher estimated cost of sampling, higher decision noise, higher adjustment rate and greater expectation of reversal.

7.4.5 Confounders

The distribution of each of the performance parameters in relation to confounders is reported in Table 7.2. Overall, performance parameters were broadly similar according to different levels of each confounder. The lowest average DTD out of all groups reported was in the group with the lowest household income (4.88). There was a slightly higher proportion of participants with low maternal education in the highest 10% of the decision noise parameter (14.9%, n=80) compared to participants from other maternal education groups (n=458, 10.3%).

7.4.5.1 Relationship between belief-updating parameters and confounding variables

Results suggest that higher cognitive processing and socio-economic status were associated with higher average DTD and less contrary updating (Table 7.2). Higher cognitive processing and socio-economic status were associated with a lower likelihood of decision noise in both tasks (Table 7.2).

In the DTD task, there was little support for an association between increased genetic risk for schizophrenia (indexed by polygenic risk score) and abnormal belief-updating. In the probability estimation task, there was some evidence to suggest that higher genetic risk for schizophrenia was associated with a greater expectation of the jars switching (OR = 1.17; 95% CI: 1.01, 1.34; p=0.031).

Table 7.2 Distribution of confounders in relation to performance parameters[1]

Belief-updating indices[1]	**Sex (Female)**			**Low Income[2]**			**Low Maternal Education[3]**			**Low IQ (bottom quintile)**			**High SCZ PRS (top quintile)**		
	Yes	No	*P*	Yes	No	*P*	Yes	No	*P*	Yes	No	*P*	Yes	No	*P*
Average DTD	4.75	5.00	<.001	4.62	4.88	<.001	4.67	4.88	0.001	4.54	4.88	<0.001	4.85	4.84	0.477
High cost of Sampling	0.27	0.23	0.013	0.25	0.26	0.337	0.26	0.25	0.256	0.26	0.26	0.434	0.26	0.25	0.923
High Decision Noise DTD task	0.11	0.10	0.350	0.14	0.10	0.008	0.14	0.10	0.009	0.17	0.10	<.001	0.11	0.11	0.548
Contrary updating	0.17	0.14	<.001	0.17	0.15	<.001	0.18	0.15	<.001	0.22	0.15	<.001	0.16	0.16	0.432
High expectation of reversal	0.11	0.09	0.027	0.12	0.10	0.015	0.11	0.10	0.150	0.16	0.10	<.001	0.13	0.10	0.031
Adjustment Rate	-0.45	-0.44	0.026	-0.44	-0.44	0.501	-0.44	-0.44	0.437	-0.43	-0.45	<.001	-0.44	-0.44	0.870
Low Confidence	0.26	0.31	0.006	0.26	0.31	0.136	0.26	0.31	0.158	0.26	0.31	0.493	0.26	0.29	0.079
High Confidence	0.34	0.37	0.091	0.34	0.37	0.672	0.34	0.37	0.960	0.34	0.37	0.233	0.33	0.35	0.501
Inference Length (1-2)	0.17	0.18	0.426	0.18	0.17	0.422	0.16	0.18	0.727	0.20	0.17	0.002	0.18	0.17	0.499
Inference Length (3-4)	0.98	0.88	0.013	0.95	0.94	0.389	0.95	0.94	0.718	0.88	0.96	0.357	0.89	0.95	0.385
Decision Noise Prob Estimation task	-3.07	-2.90	<.001	-2.90	-3.02	<.001	-2.82	-3.04	<.001	-2.68	-3.05	<.001	-3.00	-3.00	0.562

Note:[1]Binary measures: Decision noise (DTD task), cost of sampling and expectation of reversal. Continuous measures: adjustment rate, decision noise (probability estimation task). Categorical measures: confidence and inference length (compared to medium confidence & inference length 0 respectively). [2]Low income classified as bottom quintile of average income at age 33 months [3]Low maternal education classified as no GCSES.

Table 7.3 Belief-updating indices and frequent or distressing PEs at age 24 years

	Unadjusted Model			Adjusted Model[2]		
Belief-updating indices[1]	Odds Ratio	95% CI	P-value	Odds Ratio	95% CI	P-Value
Draws to Decision Task						
Average DTD	0.93	0.83, 1.06	0.273	0.97	0.86,1.10	0.671
High Cost of Sampling	0.70	0.43, 1.13	0.144	0.68	0.41,1.11	0.119
High Decision Noise	2.09	1.28, 3.42	0.003	1.71	1.02,2.87	0.043
Probability Estimation Task						
Contrary updating	1.07	0.96, 1.19	0.213	1.37	0.42,4.40	0.600
High expectation of reversal	2.47	1.53, 3.98	<.001	2.37	1.44,3.92	0.001
Adjustment rate	0.72	0.12, 4.13	0.708	0.61	0.11,3.57	0.586
High confidence	1.24	0.82, 1.87	0.307	0.99	0.72,1.35	0.927
Low confidence	0.57	0.20, 1.57	0.277	1.06	0.85,1.32	0.610
Inference Length (1-2 beads)	0.96	0.53, 1.71	0.879	1.04	0.86,1.25	0.716
Inference Length (2-4 beads)	1.11	0.73, 1.71	0.608	0.97	0.86,1.10	0.671
Decision Noise	1.12	0.93, 1.35	0.217	0.68	0.41,1.11	0.119

Note [1]Binary measures: Decision noise (DTD task), cost of sampling and expectation of reversal. Continuous measures: adjustment rate, decision noise (probability estimation task). Confidence and inference window measures are categorical measures, each with two outcomes of interest. [2]Adjusted for Working Memory, IQ, executive functioning, sex, social class, crowded living conditions, income, trauma and genetic risk for schizophrenia

7.4.6 Main Analysis

7.4.6.1 Draws to decision task and psychotic experiences

In this task, participants chose which jar the presented beads were drawn from after requesting up to ten beads. I used three indices to characterise performance: (i) the number of beads a participant requested (DTD), (ii) the subjective cost for requesting beads (cost of sampling), and (iii) how consistent performance was over the five blocks (decision noise). I used regression analyses to test their association with frequent or distressing PEs at age 24 years an outcome.

There was little evidence of an association between lower average DTD ($Beta_{crude}$= -0.00; 95% CI: -0.01,0.01; p=0.273) or the JTC bias (OR_{crude} = 1.13; 95% CI: 0.90, 1.43; p=0.297) and the likelihood of PEs. To understand belief-updating in this task, I used indices derived from computational modelling to test whether an increased estimated cost of requesting further beads or if inconsistent responses (greater decision noise) was associated with PEs. There was evidence that higher decision noise was associated with PEs (OR_{crude} = 2.09; 95% CI: 1.28, 3.42; p=0.003). This association was somewhat attenuated after adjusting for cognitive, socio-economic, genetic risk of schizophrenia and trauma (OR_{adj} 1.71, 95% CI 1.02, 2.87; p=0.043).

7.4.6.2 Probability estimation task and psychotic experiences

In this task, participants estimated the likelihood that beads were drawn from one of the jars after presented with each bead for a series of 30 beads. I used six indices of different belief-updating processes: (i) 'contrary updating' - the mean change in estimation on seeing a bead of a different colour to the ≥2 beads preceding it (ii) expectation of reversal (binary: top 10%) (iii) adjustment rate (continuous), (iv) inference length (approximate number of previous beads used to estimate the probability of the current bead presented), (v) confidence in estimations (categories: high or low), and (vi) the extent to which performance was consistent with the modelled parameters (decision noise).

Based on average revisions of estimates in response to the beads of the non-dominant colour in the sequence (contrary updating), there was little evidence of an association between an over-adjustment of estimations and PEs (OR_{adj}= 1.37; 95% CI: 0.42, 4.40; p=0.600; Table 7.3).

In analyses of the other five belief -updating measures, derived using mathematical modelling, there was evidence of an association between a higher estimated expectation that the jars that the beads are drawn from will change during the sequence (expectation of reversal measure) and a greater likelihood of being rated as having frequent or distressing PEs in the last 12 months (OR_{adj} = 2.37 95% CI: 1.44, 3.92; p=0.001). I found little evidence to support an association between the other four computational indices and PEs.

7.4.6.3 Bivariate analysis of belief-updating indices and hallucinations and delusions

To test whether the association between performance indices and PEs differed according to PEs type, I jointly modelled frequent or distressing hallucinations and delusions as two separate outcomes in a bivariate probit model. There was weaker support for an association between delusions and high decision noise (OR_{adj} = 1.50 95% CI: 0.91, 2.48: p=0.108) compared to hallucinations and high decision noise (OR_{adj} = 1.61 95% CI: 1.04, 2.50;

p=0.032). However, the Wald test comparing these estimations did not suggest a differential association between these estimates (p=0.812). Based on the Wald test p-values, there was little evidence to suggest that any of the measures were specifically associated with either hallucinations or delusions (Table 7.4).

Table 7.4 Bivariate analysis of belief-updating indices, hallucinations and delusions

Belief-updating indices[1, 2]	Odds Ratio	95% CI	P-value	Odds Ratio	95% CI	P-value	P value (hall. vs delusion)
Draws to Decision Task	Hallucinations			Delusions			
Average draws to decision	0.92	0.83 1.02	0.110	1.01	0.90, 1.13	0.905	0.186
High cost of Sampling	0.85	0.58, 1.25	0.418	0.86	0.56, 1.32	0.489	0.981
High decision Noise	1.61	1.04, 2.50	0.032	1.50	0.91, 2.48	0.108	0.812
Probability Estimation Task							
Contrary updating	1.41	0.56, 3.58	0.470	1.40	0.49, 4.01	0.525	0.996
High expectation of reversal	1.68	1.08, 2.62	0.021	2.01	1.26, 3.20	0.003	0.529
Adjustment Rate	1.03	0.25, 4.22	0.973	0.46	0.85, 1.82	0.347	0.404
Inference Window (1-2)	1.00	1.00, 1.00	0.324	1.03	0.72, 1.47	0.887	0.516
Inference Window (2-4)	1.08	0.91, 1.29	0.626	1.18	0.75, 1.85	0.474	0.553
Low confidence	1.18	0.85, 1.62	0.237	0.84	0.38, 1.85	0.664	0.322
High confidence	0.90	0.58, 1.39	0.717	1.24	0.85, 1.82	0.266	0.531
Decision Noise	1.08	0.91, 1.29	0.367	1.07	0.92, 1.26	0.364	0.939

Note: Imputed sample n=2,872 [1]Binary measures: Decision noise (DTD task), cost of sampling and expectation of reversal. Continuous measures: adjustment rate, decision noise (probability estimation task). Confidence and inference window measures are categorical measures, each with two outcomes of interest. [2]Adjusted for Working Memory, IQ, executive functioning, sex, social class, crowded living conditions, income, and genetic risk for schizophrenia and confounders. Unadjusted results are reported in the appendices

7.4.6.3 Multivariate analysis of belief -updating indices, PEs, depression and anxiety

In the multivariable probit analysis of the relationship between performance indices and PEs, depression and anxiety outcomes, there was little evidence that abnormal processes related to belief-updating are associated with a greater likelihood of symptoms of depression or anxiety (Table 7.5). Wald tests p-values that compared effect sizes between each of the three separate outcomes support that expectation of reversal in the probability estimation task is differentially associated with PEs compared to depression or anxiety (p<0.008). After adjustment for confounders, there was weaker evidence that decision noise in the DTD task was differentially associated with PEs compared to anxiety (p=0.042) or depression (p=0.056) based on model comparisons.

Table 7.5 Multivariable analysis of belief-updating indices and depression, anxiety and psychotic experiences

Belief-updating indices[1,2]	Odds Ratio Depression	95% CI	P value	Odds Ratio PEs	95% CI	P-value	Odds Ratio Anxiety	95% CI	P - value	P-value Dep. vs PEs	P-value Anx. vs PEs	P-value Anx. vs Dep.
Draws to Decision Task												
Average draws to decision	0.90	0.92, 1.06	0.698	0.97	0.89, 1.06	0.541	1.04	0.97, 1.11	0.541	3231	0.377	0.241
High cost of Sampling	1.11	0.86, 1.43	0.413	0.76	0.54, 1.06	0.107	0.93	0.73, 1.18	0.107	0.163	0.416	0.248
High decision Noise	0.98	0.68, 1.42	0.928	1.60	1.08, 2.35	0.018	1.21	0.87, 1.66	0.255	0.056	0.042	0.437
Probability Estimation Task												
Contrary updating	0.97	0.90, 1.04	0.414	1.01	0.93, 1.10	0.756	0.98	0.92, 1.05	0.414	0.660	0.771	0.683
High expectation of reversal	1.22	0.86, 1.72	0.271	1.83	1.25, 2.68	0.002	0.97	0.69, 1.37	0.882	0.006	0.007	0.443
Adjustment Rate	0.95	0.34, 2.61	0.917	0.70	0.20, 2.45	0.576	1.03	0.41, 2.62	0.949	0.847	0.854	0.988
Inference Window (1-2)	0.92	0.68, 1.24	0.567	0.93	0.64, 1.35	0.704	1.09	0.83, 1.43	0.527	0.808	0.545	0.737
Inference Window (2-4)	1.07	0.86, 1.34	0.545	1.09	0.82, 1.43	0.561	0.94	0.76, 1.15	0.538	0.729	0.665	0.536
Low confidence	0.62	0.37, 1.05	0.077	0.58	0.30, 1.15	0.121	0.88	0.58, 1.35	0.567	0.083	0.279	0.208
High confidence	1.16	0.91, 1.49	0.224	1.21	0.90, 1.64	0.207	0.96	0.76, 1.21	0.747	0.251	0.402	0.323
Decision Noise	0.97	0.87, 1.08	0.569	1.09	0.95, 1.24	0.214	1.24	0.89, 0.98	0.631	0.344	0.820	0.372

Note [1]Binary measures: Decision noise (DTD task), cost of sampling and expectation of reversal. Continuous measures: adjustment rate, decision noise (probability estimation task). Confidence and inference window measures are categorical measures, each with two outcomes of interest. [2]Adjusted for Working Memory, IQ, executive functioning, sex, social class, crowded living conditions, income, and genetic risk for schizophrenia. Unadjusted results are reported in the appendices

Table 7.6 Exposure to trauma (age 0-17 years) and belief-updating indices

Belief-updating indices[1]	Unadjusted Model Effect Size	95% CI	P-Value	Adjusted Model[2] Effect Size	95% CI	P-Value
Draws to Decision Task						
Average Draws to decision	-0.07	-0.12, -0.02	0.009	-0.06	-0.11, -0.00	0.035
High Cost of Sampling	1.00	0.93, 1.08	0.980	1.00	0.92,1.08	0.927
High Decision Noise	1.18	1.06, 1.32	0.002	1.15	1.03,1.29	0.012
Probability Estimation Task						
Contrary updating	0.04	-0.02, 0.09	0.189	0.01	-0.04,0.07	0.610
Expectation of reversal (top 10%)	0.99	0.88, 1.10	0.802	0.97	0.87,1.09	0.618
Adjustment rate	0.00	-0.00, 0.01	0.095	0.00	-0.00,0.01	0.128
Inference window (1-2 beads)	0.99	0.92, 1.06	0.739	0.95	0.83,1.09	0.477
Inference window (2-4 beads)	0.97	0.85, 1.11	0.662	1.38	0.66,2.92	0.394
High confidence	0.94	0.85, 1.04	0.208	1.03	0.87,1.22	0.757
Low confidence	0.96	0.89, 1.03	0.216	1.01	0.61,1.66	0.977
Decision noise	0.07	0.03, 0.10	<.001	0.050	0.02,0.08	0.005

Note: Imputed sample n=2,872 [1]Binary measures (odds ratio reported): Decision noise (DTD task), cost of sampling and expectation of reversal. Continuous measures: adjustment rate, decision noise (probability estimation task; beta co-efficient reported). Confidence and inference window measures are categorical measures, each with two outcomes of interest (odds ratio reported). [2]Adjusted for sex, income, crowding, social class and maternal education.

7.4.6.4 Exposure to trauma and abnormal belief-updating processes

In this analysis belief-updating indices were analysed as an outcome in relation to exposure to trauma during childhood. There was evidence of an association between exposure to a greater number of trauma types between age 0-17 years and greater decision noise in the DTD task (OR_{adj} =1.15, 95% CI: 1.03, 1.29; p=0.012; Table 7.6). When additionally adjusting for cognitive functioning (working memory, executive processing, IQ), this association was minimally attenuated (linear trend: OR_{adj} = 1.14; 95% CI = 1.02, 1.30; p=0.021).

In the probability estimation task, there was also evidence that exposure to trauma was associated with a greater likelihood of higher decision noise (OR_{adj} = 0.05; 95% CI = 0.02, 0.08; p=0.005) that was not substantially reduced by additional adjustment for cognitive functioning (OR_{adj} = 0.04; 95% CI = 0.01, 0.08; p=0.016).

7.4.6.5 Mediation analysis

Decision noise in the DTD task was associated with trauma and PEs in earlier analyses; therefore, I selected this parameter for mediation analysis. Exposure to three or more types of trauma increased the risk of PEs at age 24 years by 3.11 times (adjusted for maternal education; 95% CI: 2.04, 4.74). There was little evidence to suggest that the association between exposure to multiple types of trauma (3+) and PEs is mediated by decision noise on the DTD task (Natural Indirect Effect OR_{adj} = 1.03; 95% CI = 0.99, 1.08; % mediated <1%; (Table 7.7).

Table 7.7 Mediation analysis of trauma (exposure to 3+ trauma types), higher decision noise (draws to decision task) and PEs at age 24 years

	Odds ratio	95% CI
Controlled direct effect	3.02	1.98, 4.61
Natural indirect effect	1.03	0.99, 1.08
Marginal total effects	3.12	2.05, 4.76

Note: all estimations adjusted for maternal education; imputed sample (n=2,872)

7.4.7 Sensitivity Analysis

7.4.7.1. Belief-updating processes and different definitions of PEs outcome

To test whether my findings differed according to the definition of PEs used in analyses, I repeated the main analysis using a broader definition (any suspected or definite PEs in the last 12 months) and a narrower definition (psychotic disorder) of PEs. There was little evidence to suggest that any of the belief-updating indices were associated with a broader outcome of any past-year suspected or definite PEs (Table 7.8).

There was an association for both decision noise in the DTD task (OR_{adj}=2.24; 95% CI: 1.15, 4.38; p=0.018) and increased expectation of reversal in the probability estimation task (OR_{adj}= 2.89; 95% CI: 1.50, 5.54; p=0.001) with an increased risk of psychotic disorder (Table 7.9). These estimated effect sizes were slightly greater compared to analyses with frequent or distressing PEs (decision noise DTD task: OR_{adj}= 1.71, 95% CI: 1.02, 2.87; p=0.043: expectation of reversal: OR_{adj} = 2.37; 95% CI: 1.44, 3.92; p=0.001).

Table 7.8 Belief-updating indices and suspected or definite PEs in the past 12 months

Belief-updating indices[1]	Unadjusted Model Odds Ratio	95% CI	P-value	Adjusted Model[2] Odds Ratio	95% CI	P-Value
Draws to Decision Task						
Average DTD	0.91	0.82,1.00	0.051	0.92	0.84,1.02	0.124
High cost of Sampling	1.02	0.72,1.45	0.907	1.01	0.71,1.44	0.964
High decision Noise	1.59	1.03,2.43	0.035	1.42	0.90,2.22	0.128
Probability Estimation Task						
Contrary updating	0.99	0.90,1.09	0.881	0.78	0.28,2.18	0.638
High expectation of reversal	1.35	0.86,2.14	0.194	1.37	0.86,2.21	0.187
Adjustment Rate	0.92	0.23,3.67	0.902	0.81	0.20,3.32	0.770
Confidence (high or low)	1.08	0.85,1.38	0.526	1.09	0.85,1.40	0.483
Inference Length	0.93	0.78,1.10	0.369	0.93	0.78,1.10	0.387
Decision Noise	1.04	0.90,1.20	0.620	0.98	0.84,1.14	0.749

Note: Imputed sample (n=2,872) [1]Binary measures: Decision noise (DTD task), cost of sampling and expectation of reversal. Continuous measures: adjustment rate, decision noise (probability estimation task). Categorical measures: Confidence and inference window measures [2]Adjusted for Working Memory, IQ, executive functioning, sex, social class, crowded living conditions, income, genetic risk for SCZ, exposure to trauma and maternal education

Table 7.9 Belief-updating indices and psychotic disorder

Belief-updating indices[1]	Unadjusted Model Odds ratio	95% CI	P-value	Adjusted Model[2] Odds ratio	95% CI	P-Value
Draws to Decision task						
Average DTD	0.86	0.72,1.02	0.077	0.90	0.76,1.07	0.232
High cost of Sampling	0.81	0.43,1.55	0.529	0.78	0.41,1.50	0.459
High decision Noise	2.66	1.41,5.01	0.003	2.24	1.15,4.38	0.018
Probability Estimation Task						
Contrary updating	1.07	0.92,1.24	0.388	1.33	0.26,6.93	0.733
Higher expectation of reversal	3.07	1.65,5.70	<.001	2.89	1.50,5.54	0.001
Adjustment Rate	0.43	0.04,5.14	0.508	0.38	0.03,4.56	0.444
Confidence (high or low)	1.22	0.81,1.83	0.348	1.22	0.81,1.84	0.350
Inference Length	1.09	0.81,1.47	0.560	1.09	0.81,1.48	0.575
Decision Noise	1.20	0.93,1.55	0.160	1.09	0.84,1.42	0.517

Note: Imputed sample (n=2,872) [1]Binary measures: Decision noise (DTD task), cost of sampling and expectation of reversal. Continuous measures: adjustment rate, decision noise (probability estimation task). Categorical measures: Confidence and inference window measures [2]Adjusted for Working Memory, IQ, executive functioning, sex, social class, crowded living conditions, income, genetic risk for schizophrenia, exposure to trauma and maternal education

7.4.7.2 Complete-case analysis

I repeated the main analyses using the complete-case sample, which included participants who had complete data for PEs, trauma, confounding variables and the beads tasks. There were some differences in findings between imputed data and complete-case data (n=1,652; Appendix Table 5.2). There was little evidence of a relationship between a greater expectation of reversal and an increased likelihood of PEs (OR_{adj} = 0.93; 95% CI: 0.78,1.11; p=0.432), which was observed in the analysis of imputed data (OR_{adj} = 2.28; 95% CI: 1.39, 3.74; p=0.001).

In the complete-case analysis of exposure to trauma and belief-updating indices as an outcome (Appendix Table 5.3), there was little evidence to support an association between exposure to trauma and any of the belief-updating indices. This includes decision noise in the DTD task (decision noise: $Beta_{adj}$ = 0.03; 95% CI: -0.02, 0.07; p=0.149), whereas there was some support for this association in the imputed dataset ($Beta_{adj}$ = 0.050; 95% CI: 0.02,0.08; p=0.005).

7.5 Discussion

7.5.1 Belief-updating and confounding variables

My analysis of the relationship between belief-updating processes and potential confounding variables support previous findings that lower socioeconomic status (Baker, Konova, Daw, & Horga, 2019) and poorer cognitive functioning (Jolley et al., 2014; Stuke et al., 2017) are associated with lower DTD. I also found evidence that high decision noise in both tasks was associated with lower socioeconomic status and poorer cognitive functioning. This finding highlights the importance of using study designs or analytical methods that take potential confounders into account when investigating the causal relationship between indices of performance on the beads task and PEs.

A previous study had found evidence of an association between family history of psychotic disorder and an increased likelihood of the JTC bias (Van Dael et al., 2006). I did not find evidence to support a relationship between genetic risk for schizophrenia and lower DTD, which was similarly reported in a recent analysis of a large general population sample (Tripoli et al., 2020). For computational indices, there was little support for an association between increased genetic risk of schizophrenia and abnormal belief-updating indices, a relationship that has not been investigated, to my knowledge, in previous studies.

7.5.2 Belief-updating processes and PEs

After adjustment for confounders, people with PEs were 1.71 times more likely to have sub-optimal or inconsistent belief-updating (indexed by high decision noise) in the DTD task and 2.37 times to have an increased expectation that an outcome will change (indexed by an increased expectation of reversal) in the probability estimation task. The minimal attenuation by confounders suggests that the association between abnormal belief-updating processes and PEs is not explained by cognitive functioning, socio-economic status or genetic risk of schizophrenia. These results contribute to previous findings from clinical studies, which may have been less able to rigorously control for confounding, by providing evidence that confounding does not account for the relationship between abnormal belief-updating processes and psychosis-related outcomes (Adams et al., 2018; Ermakova et al., 2017; Moutoussis et al., 2011).

My results do not suggest that there is an association between a higher cost of sampling and PEs in the DTD task. This finding suggests that people with PEs are not consistently estimating a higher ‘cost’ of requesting further beads due to motivational factors. This finding is consistent with previous studies that have not found evidence to support an association between an increased ‘need for closure’ and the JTC bias (Colbert & Peters, 2002; McKay, Langdon, & Coltheart, 2006).

There was also a lack of association between several potentially abnormal belief-updating processes and PEs. These indices include how much previous evidence was used to make a new estimation (inference window), how rapidly estimations were revised (adjustment rate) and levels of confidence in estimation (high or low confidence). It is possible a lack of association is due to a lack of statistical power, however it is unlikely that this is the case based on the large sample size. These findings suggest that only specific aspects of belief-updating (i.e. an increased expectation of reversal) are likely to differ according to PEs outcome. The lack of evidence for an association between general learning rate (indexed by adjustment rate) and psychosis-related outcomes is also in line with previous studies that have tested similar indices (Adams et al., 2018; Stuke et al., 2017).

In a study of the DTD task and PLEs in a small general population sample (n=98), Stuke and colleagues (2017) found that evidence of an association between PLEs and a maladaptive learning strategy indicative of poor predictive processing (low resilience against irrelevant information). This maladaptive learning style could be an abnormal belief-updating process that accounts for the association between increased decision noise and PEs in my results.

People with psychosis-related outcomes are more likely to be resistant to contradictory evidence in studies that use situational judgement paradigms (Eisenacher et al., 2016; Woodward, Buchy, Moritz, & Liotti, 2007). However, this is in contrast with results from the probability estimation task in my study and previous studies, that find an association between both greater expectation of change and increased revision of beliefs and PEs (Fear & Healy, 1997). Based on a hierarchical model of information processing organised according to complexity (Chapter 2; Broyd, Balzan, Woodward, & Allen, 2017), unstable and changing belief-updating (e.g. decision noise, expectation of reversal) may occur at a low level of the information-processing hierarchy (e.g. estimating probability on a simple outcome) and contribute to poor predictive processing. Lower-level abnormal processes may then inform higher-level abnormal belief-updating (e.g. a bias against revising beliefs about the cause of an event or social cognition) that contribute to the development of delusional beliefs that are resistant to contrary information. Abnormal belief-updating may also contribute to the attribution of increased significance to irrelevant stimuli (aberrant salience), an abnormal perceptual process observed in the prodromal stages of psychosis (Kapur, 2003).

In addition to analyses of computational indices, I analysed behavioural indices of abnormal belief-updating – average DTD, the JTC bias, contrary updating –to compare findings to previous studies. There are mixed findings from studies of the relationship between the JTC bias and PLEs in general population samples. In a meta-analysis of studies of general population samples, confidence intervals for 16 out of 23 (69%) included studies crossed the null value and reported that there is a weak association between DTD and PLEs (Ross et al., 2015). This meta-analysis was based on small samples (average n=59), which may have led to a lack of statistical power to detect an effect in some included studies. The meta-analysis did not provide a quality assessment of included studies; therefore, several sources of bias may have contributed to heterogeneity in results. In a subsequent study, Ross and colleagues (2016) did not find an association between lower DTD and PLEs in a sample that completed the task online (n=558). In a general population sample (n=1,294), there was a lack of evidence to suggest that delusions or hallucinations (assessed by a diagnostic checklist) were associated with a lower DTD (Tripoli et al., 2020). However, Tripoli and colleagues found an association between positive PLEs (assessed using the CAPE questionnaire) and lower DTD. The inconsistency of findings according to PLE measure in Tripoli and colleague's study suggest that potential measurement error of PLEs may contribute to these observed results. The use of PLEs collected by self-report in previous studies is likely to contribute to increased measurement error compared to the measurement of PEs using semi-structured interviews as I have used in this study.

My results do not provide evidence of an association between a lower DTD and PEs in a general population sample. As previous studies have also not found evidence of an association between lower DTD and psychosis-related outcomes, my study may strengthen the claim that behavioural indices from performance on the DTD task are of limited replicability and reliability (Moritz et al., 2017) and indices of derived from computational modelling may be of greater value in this area. Sources of variation between studies may contribute to heterogeneity in the evidence base; for example, the use of different ratios of colour beads leads to variations in task difficulty. Both Ross (2016) and Tripoli and colleagues (2020) used 60:40 ratios of coloured beads (increasing task difficulty compared to 80:20 ratio) in their version of the task and participants completed a single block, which are key methodological differences to the DTD task used in this chapter (80:20 ratio coloured beads and five blocks). As the instructions given by researchers for the task vary across studies, task incomprehension may also contribute to inconsistent findings between studies.

Previous studies have reported an association between greater contrary updating (average revision of probability in response to new evidence) and psychotic symptoms (Colbert and Peters 2002; Fear and Healy 1997; Rodier et al. 2011; So and Kwok 2015; Ward et al. 2018). Results from studies of contrary updating in general population samples have been inconsistent and based on small sample sizes (n <100; Howe, Ross, McKay, & Balzan, 2018; Rodier et al., 2011). My findings do not suggest that there is an association between greater contrary updating and PEs in a large population sample and may suggest that previous studies may have overestimated the association between contrary updating and psychotic symptoms due to sources of bias or confounding.

7.5.3 Belief-updating processes and psychiatric symptom specificity

Analyses that jointly modelled delusions and hallucinations did not suggest that the associations with measures of performance on either task are specific to sub-clinical delusions or hallucinations. Findings from the bivariate model are inconsistent with some theoretical models (Bentall & Fernyhough, 2008; Broyd et al., 2017) and empirical studies of the beads task (Ross et al., 2015) that suggest that the JTC bias is specifically associated with delusions and not hallucinations. My finding that abnormal belief-updating processes are associated with both sub-clinical hallucinations and delusions suggests that there are shared abnormal belief-updating processing that contributes to both hallucinations and delusions. This may be interpreted as being in line with the predictive processing account of psychosis, which suggests that impaired predictive processing may contribute to both the development of hallucinations and delusions (Fletcher & Frith, 2009; Sterzer, Voss, et al., 2018).

I also aimed to establish whether abnormal belief-updating processes are associated with non-psychotic psychopathology, indexed by symptoms of depression and anxiety. The lack of support for an association between abnormal belief-updating and non-psychotic psychopathology suggest that these biases may be specific to symptoms of psychosis. This result is in line with meta-analytic findings of the beads task that suggest that differences in probabilistic inference are not associated with non-psychotic psychiatric outcomes (So et al., 2016).

There was little evidence that the indices were associated with broader measures of PEs (suspected or definite PEs). As the broader measure of PEs is likely to include more participants who are misclassified as having true PEs, it was anticipated that the relationship between abnormal belief-updating and PEs would be weaker compared to narrower measures of PEs (frequent or distressing PEs). The estimated effect size for the association between abnormal belief-updating processes (decision noise, the expectation of reversal) and PEs that met the clinical threshold for psychotic disorder was greater than frequent or distressing PEs; this finding strengthens the findings from the main analysis.

7.5.4 Exposure to trauma and abnormal belief-updating

There was evidence to suggest that exposure to trauma was associated with increased decision noise in both versions of the beads task. There was a lack of support for an association between exposure to trauma and abnormal belief-updating modelled by the ‘costed Bayesian model’ (cost of sampling) in the DTD task or the HMM model (expectation of reversal, adjustment rate, inference length, estimation confidence) in the probability estimation task. The association between trauma and decision noise in both tasks was not explained by socio-demographic measures or cognitive functioning.

The strength of the relationship between exposure to trauma and decision noise on both tasks increased according to the number of types of trauma reported between ages 0-17 years, which suggests that polyvictimisation is associated with the greatest increase in the likelihood of high decision noise at age 24 years. This finding suggests that exposure to trauma contributes to an alteration in how information is processed, which may be more inconsistent or based on a sub-optimal strategy that is not modelled in the analysis. As was previously found in a small general population sample, I found little evidence of an association between exposure to trauma and average draws to decision on the beads tasks (Freeman et al., 2008). No studies, to my knowledge, have investigated the relationship between exposure to trauma and performance on versions of the beads task using indices derived using mathematical modelling.

There is evidence to suggest that exposure to trauma during childhood is associated with abnormal brain development that contributes to cognitive impairment and an increased risk of psychopathology (Edwards, 2018; Gur et al., 2019; Perry et al., 1995). The association between exposure to trauma and higher decision noise may be an indicator of the developmental impact of trauma on brain development. As the relationship between trauma and sub-optimal belief updating was not accounted for by cognitive functioning, it may suggest that there are neurological effects of trauma on the developing brain that are not indexed by cognitive ability. However, as cognitive functioning was assessed at age eight years, there is some uncertainty in this finding (i.e. cognitive functioning at a later time-point may explain the association). This finding may have transdiagnostic implications for understanding the effects of childhood trauma on cognition and a potential neural basis for my findings could be examined in future studies using brain-imaging analyses.

In the predictive processing model, a sub-optimal ability to update beliefs in response to an environment reduces the ability to make accurate predictions about the world, which can make new environments seem unpredictable and could lead to mental distress. Impaired belief-updating may be associated with maladaptive psychological mechanisms (e.g. negative cognitive schema, threat-related perceptual biases, external attribution bias; see chapter 2) that are hypothesised to be on the pathway from trauma to the development of mental health disorders.

7.5.5 Mediation analyses

Based on my finding that decision noise was associated with both exposure to trauma and an increased likelihood of PEs, I investigated whether decision noise is a potential mediator between exposure to trauma and PEs at age 24 years. There was little evidence to support the claim that decision noise mediated this relationship. This finding was contrary to my hypothesis, which was informed by theoretical models that suggest abnormal belief-updating processes contribute to the causal pathway from trauma to an increased risk of psychosis-related outcomes.

However, there are several limitations in what can be inferred from the mediation analysis. Decision noise is not an index of a specific abnormal belief-updating process, and high decision noise suggests that participants are using a sub-optimal, unmodelled belief-updating strategy. It is unlikely that the measure of high decision noise is indicative of a single belief-updating process, but rather several processes not modelled by the ‘costed Bayesian model’ (e.g. random responses, non-linear learning rate, confidence). Therefore, I was not able to test a specific belief-updating strategy that could be on the pathway from trauma to PEs indexed by the DTD model. The results of the probability estimation task did not suggest there was a computational index of abnormal belief-updating that was associated with both exposure to trauma and an increased likelihood of PEs.

Few studies have investigated possible mediators related to belief-updating in the relationship between exposure to trauma and PEs. In a general population sample, Gawęda and colleagues (2018) derived a latent characteristic of several processes relating to social cognition and information-processing biases (attention to threat, external attribution, safety behaviours) and reported that this characteristic along with symptoms of self-disorders (i.e. feelings of a weakened sense of self) partially mediated (51% mediated) the relationship between trauma and PLEs in a general population sample. However, this study assessed information-processing biases using a self-report questionnaire and is unlikely to be comparable to the indices of belief-updating used in my study. Furthermore, these findings are limited by a lack of adjustment for confounders and it is not clear how much of the mediated effect was mediated by symptoms of self-disorder.

7.5.6 Strengths and limitations

By using indices of belief-updating derived from computational models I was able to compare findings to those from studies that have used a similar methodological approach in small clinical samples. I contributed to the current literature by applying these methods to a large cohort sample and addressing the limitations of prior studies. I was also able to compare results from other general population samples and inform previous findings by analysing behavioural indices from the two versions of the beads task.

Thanks to the availability of data from participants in the ALSPAC cohort, I was able to address the limitations in the current evidence base by testing the role of confounding between abnormal belief-updating and PEs using measures of several potential confounders (genetic risk of schizophrenia, socio-demographic background, cognitive functioning). Using these measures, I was able to establish that my findings for both trauma and PEs were unlikely to be accounted for by confounding.

A methodological limitation for several studies is the use of self-report questionnaires that are more prone to measurement error than interview-based assessments (Linscott & Os, 2013). The use of a semi-structured interview for the assessment of PEs (PLIKSi) in my study increased the validity of the measure of PEs (see discussion in chapter 1).

For my analysis of abnormal belief-updating processes and PEs, both measures were assessed simultaneously, which inhibits inferring causal implications from the results. I was unable to rule out possible reverse-causal effects (i.e. PEs contribute to abnormal belief-updating). In clinical samples, there is evidence to suggest that performance on the beads task (the JTC bias) is stable when measured at different timepoints (Peters & Garety, 2006; Winton-Brown et al., 2015), which warrants further investigation of the longitudinal association between abnormal belief-updating the development of psychosis-related outcomes.

As was also the case for study I, I used measures of trauma relating to several different types of trauma exposure that were collected throughout early life (0-17 years of age) from multiple sources and at multiple timepoints. By using these measures of trauma exposure, I was able to test whether exposure to trauma was associated with an increased likelihood of abnormal belief-updating at age 24 years. The use of longitudinal data for this part of the study strengthens the conclusion that trauma contributes to subsequent changes in belief-updating; this was also supported by the detection of a dose-response relationship between the number of trauma types experienced and an increase in the likelihood of decision noise, which is consistent with a causal relationship (Hill, 1965).

As discussed in chapter 3, a previous study of the probability estimation task reported that miscomprehension of the task accounted for increased contrary updating (Balzan, Delfabbro, Galletly, & Woodward, 2012). For study III, ALSPAC field workers were instructed to confirm that participants understood the task and participants completed a trial run of each of the beads tasks (DTD and probability estimation) to minimise task incomprehension. It is unclear whether individuals with symptoms of psychopathology (PEs, anxiety, depression) or those who been exposed to trauma may have been more likely to misunderstand instructions for the tasks; if this is the case, it will contribute to differential measurement error and bias results.

As is the case with most cohort studies, there is a risk of bias from attrition to consider when interpreting these results. For the sample that had data on the beads tasks and PEs, I used multiple imputation to predict missing values using a wide range of auxiliary factors that were associated with attrition. There were some differences in results between the complete-case and imputed samples including a lack of evidence for an association between an increased expectation of reversal and PEs in the complete-case sample, an association that was detected in the imputed sample. The complete-case sample is more likely to be affected by attrition bias than the imputed sample and, therefore, results from the imputed sample are more likely to be more reliable. If both abnormal belief-updating and PEs contribute to missingness in the complete-case sample, this may lead to an underestimation of effects that could account for the weaker effects found in the complete-case sample.

While computational modelling does have the potential to provide greater insight into the mechanisms that drive behavioural differences, there are some limitations to applying this approach. For the DTD task, the amount of data collected was limited to five blocks (providing five data-points) completed by the participants, which meant that it was only feasible to fit two indices (cost of sampling and decision noise) to the data. For the probability estimation task, a model with more parameters could be fitted to the data because participants estimated the likelihood of which jar the beads were drawn from 30 times (providing 30 data-points). If participants had completed additional blocks of the DTD task, thus providing more data-points, it might have been possible to test other computational models to fit the data, and examine other indices of belief-updating processes (e.g. non-linear updating; Stuke et al., 2017) that could potentially provide a greater understanding of the underlying processes that drive performance on the task. A final limitation, as discussed previously, is that the decision noise parameter is not an index of a specific abnormal belief-updating process; therefore, findings related to this parameter are limited in how they can inform our understanding of belief-updating processes related to trauma or PEs.

7.5.7 Implications

Abnormal belief-updating may be a marker of an increased risk of PEs and could be a mechanism that informs the content of integrated models of psychosis. If it is the case that abnormal belief-updating processes have a causal effect on the development of PEs, these processes could provide novel targets for interventions if they are modifiable. My findings also suggest that abnormal belief-updating is unlikely to be a transdiagnostic marker of vulnerability to more common mental health outcomes (i.e. anxiety or depression) but that it may be specific to PEs.

The lack of evidence for an association between behavioural indices of abnormal belief-updating (i.e., the JTC bias, lower DTD, contrary updating) and PEs or psychotic disorder in a large general population sample using a semi-structured interview assessment of PEs - challenges the validity of previous findings, particularly as sample size and risk of measurement error were important limitations of several previous studies. My findings suggest that the use of computational modelling can nevertheless provide evidence of abnormal belief-updating mechanisms in those with PEs even when they not detected by behavioural indices, and this could inform future studies of cognitive mechanisms and psychosis-related outcomes.

7.5.7.1 Exposure to trauma and belief-updating abnormalities

Results from this chapter also suggest that exposure to trauma in childhood and adolescence increases the likelihood of sub-optimal belief-updating at age 22 years, as indexed by increased decision noise in both tasks, and the evidence of a dose-response relationship that does not appear to be explained by confounding or reverse causation is consistent with a causal effect. This relationship warrants further investigation in future studies to establish what specific effects trauma has on belief-updating and how these may contribute to mental health outcomes.

Recent theoretical and computational papers have developed a model of trauma and the development of PTSD in a predictive processing model (Kaye, Kwan, Ressler, & Krystal, 2019; Linson, Parr, & Friston, 2019; Wilkinson, Dodgson, & Meares, 2017). In this model, exposure to a traumatic event alters normative predictive processing by establishing a learned association between exposure to threat and unrelated stimuli (non-associative learning). This learned association alters prior expectations in new environments and may make ambiguous stimuli more likely to seem threatening. The consequent alteration in belief-updating is characterised as a state of ‘self-maintaining threat preparedness’ that inhibits individuals from appropriately ‘reality-testing’ whether an environment is threatening and being able to update their beliefs in light of new evidence (Linson & Friston, 2019). My findings lend support to this model by providing evidence of an association between exposure to trauma and sub-optimal belief-updating. While I found little support for an association between abnormal belief-updating and symptom of depression or anxiety, I did not investigate whether abnormal belief-updating is associated with PTSD, an outcome that commonly overlaps with PEs (Hardy, 2017). Therefore, it is not known whether increased decision noise, as examined in this chapter, is associated with PTSD. Future studies could investigate whether specific belief-updating processes mechanisms are causally associated with exposure to trauma during childhood.

7.5.7.2 Mediation Analyses

My results suggest that decision noise (indexed in the DTD task) is unlikely to mediate the association between trauma and PEs. As discussed in the previous section, there are limitations to what can be inferred from the results of the mediation analysis as decision noise is not a measure of a single abnormal belief-updating process. Further studies should aim to identify abnormal belief-updating processes not tested in study III and, based on previous literature, could mediate the relationship between exposure to trauma and PEs including reward processing, reinforcement learning and attribution of salience (Barch et al., 2017; Boehme et al., 2015; Pechtel & Pizzagalli, 2013; Roiser et al., 2013; Waltz et al., 2015).

It may also be the case that abnormal belief-updating is not on the pathway from trauma to PEs. This finding would challenge integrated bio-psycho-social models, namely the dopamine model, which suggests that exposure to environmental stressors contribute to altered information processing via dysregulated dopamine activation that, in turn, contributes to an increased risk of PEs. To my knowledge, there is an absence of studies that have investigated the association between dysregulated dopamine activation and abnormal belief-updating; therefore, this theoretical claim might be unfounded.

7.6 Conclusion

The results of this chapter provide evidence of an association between abnormal belief-updating processes (increased expectation of change, decision noise) and an increased likelihood of PEs. These findings suggest that there are abnormal belief-updating characteristics that occur before the development of psychotic disorder that can be detected using computational modelling of performance on probabilistic reasoning tasks in a general population sample. Longitudinal studies are required to infer the potentially causal role that these abnormal belief-updating processes may have in the development of symptoms of psychosis.

I also found evidence of a dose-response relationship between exposure to childhood trauma and subsequent greater decision noise, consistent with a causal relationship between exposure to trauma and sub-optimal decision making. This finding lends support to the predictive processing account of trauma that claims exposure to trauma contributes to an impairment in reality-testing.

There was little evidence to support the hypothesis that greater decision noise mediates the relationship between exposure to trauma and PEs, which is not consistent with theoretical models that suggest that abnormal belief-updating processes are on the causal pathway between exposure to trauma and an increased risk of PEs.

Chapter 8 Discussion

8.1 Overview

In this thesis, I have aimed to test the hypothesis that exposure to trauma is causally related to PEs and that information-processing biases are on this causal pathway. I have addressed these aims by analysing data from the ALSPAC cohort (studies I & III) and conducting a systematic review and meta-analysis of prior literature in the area (study II).

8.1.1 Study I: Exposure to trauma and PEs

In study I, I found evidence that the risk of PEs at age 18 years was increased by approximately 3-fold following exposure to trauma during childhood or adolescence. The risk of PEs for participants who were exposed to three or more different types of trauma during childhood or adolescence was increased almost 5-fold. These effects are in line with previous findings from cross-sectional and longitudinal studies (Gibson et al., 2016; Varese et al., 2012). The associations between trauma and PEs were not explained by potential sources of confounding (sex, genetic risk of psychopathology, developmental delay and socio-economic status), which is also consistent with previous research (Arseneault et al., 2011; De Loore et al., 2007; Spauwen et al., 2006; Varese et al., 2012).

My findings develop the previous evidence base (Chapters 1 and 2) by providing evidence that suggests different types of interpersonal violence and neglect are associated with subsequent PEs before and after adjustment for environmental and genetic confounders; these findings are consistent with previous longitudinal studies that have tested some types of trauma but had not comprehensively adjusted for confounding (e.g. Arseneault et al., 2011; De Loore et al., 2007; Kelleher et al., 2013). My finding, that different types of trauma are associated with PEs, after adjusting for both different types of trauma exposure and confounders in a multivariable model are consistent with previous findings from a large cross-sectional study (McGrath et al., 2017). Some previous studies have interpreted their findings to suggest that specific types of interpersonal violence or neglect are associated with a greater risk of PEs (Abajobir et al., 2017; Bentall et al., 2012). Contrary to claims of specific effects of trauma types on PEs risk, my results support the thesis that there is a shared pathway by which different types of trauma affect the risk of PEs.

In my analysis of exposure to trauma and PEs according to different age-periods of exposure (early childhood, mid-childhood, adolescence), there was a lack of evidence to support the view that there are critical or vulnerable age-periods where exposure to trauma differentially increases the risk of PEs. I did some find evidence to suggest that there is an elevated effect of recent trauma on the risk of PEs compared to trauma exposure during earlier age-periods. Similar recency effects have been reported in a cohort study examining exposure to bullying and PLEs (Kelleher et al., 2013).

In line with several previous studies, I found evidence of a dose-response relationship between trauma exposure and risk of PEs (Arseneault et al., 2011; Bentall et al., 2012; De Loore et al., 2007; McGrath et al., 2017; Moriyama et al., 2018; Shevlin et al., 2008; Lataster et al., 2006). I extended the current evidence base by finding evidence of this dose-response relationship for trauma exposure for each age-period tested (early childhood, mid-childhood, adolescence). The dose-response effect of trauma on PEs was also present when using an index of dose based on the number of age-periods that exposure to trauma was experienced.

In the allostatic load model of stress, exposure to extreme stress has been shown to have a widespread effect on systems that regulate the brain's capacity to adapt to stress (e.g. metabolic, immune and cortisol systems; McEwen et al., 2015). The chronic activation of stress management systems can cause alterations to neuronal structure and brain connectivity that can become pathogenic and contribute to the risk of adverse physical and mental health outcomes, including psychosis (Alastalo et al., 2009; Chen et al., 2006; Savransky et al., 2018). Exposure to chronic stress has a developmental impact in early life by the 'biological embedding' of long-term maladaptive stress responses (Gunnar et al., 2009; Lupien et al., 2009; Rogosch et al., 2011; Shonkoff et al., 2009). By understanding PEs as a maladaptive response to stress, my findings are consistent with the allostatic load model by providing evidence of the long-term developmental ('embedding') effects of trauma on later PEs; the effects of which are heightened by immediate stress (recency effects) and worsened by chronic exposure (dose-response effect).

The common pathway from multiple stressors to an increased risk of PEs may have implications for exposure to other environmental stressors associated with an increased risk of PEs. In a study of Swedish registry data, refugees had a greater risk of psychotic disorder compared to non-refugee migrants (Hollander et al., 2016), which may be explained by a dose-response effect of both social stressors from migration and the greater likelihood of exposure to trauma for refugees compared to other groups (Betancourt et al., 2017; Tinghög et al., 2017). In a case-control study of individuals with psychotic disorder, exposure to both childhood urbanicity and trauma increased the likelihood of psychotic disorder in a dose-response manner; urbanicity was also associated with a greater risk of childhood trauma (Frissen et al., 2015). These findings illustrate the potential contribution of trauma exposure to other environmental risk factors for psychosis that could be investigated in future studies.

8.1.2 Study II: Exposure to trauma and information-processing biases

As discussed in chapter 2, theoretical models of psychosis claim that exposure to trauma increases the likelihood of several information-processing biases that, in turn, increase the risk of psychosis. To develop the current evidence base for these theoretical claims, I conducted a systematic review and meta-analysis of previous studies that have investigated the relationship between trauma and psychosis-related information-processing biases.

I did find some evidence to suggest that exposure to childhood trauma is associated with a greater likelihood of a bias towards attributing the cause of different outcomes to external factors (external LOC), which is a risk factor for a wide range of negative mental health and social outcomes (Nowicki, 2016). This suggests that a bias for an external LOC could be a potential mechanism on the pathway from trauma to psychotic symptoms. However, the evidence was highly heterogeneous and of mixed quality, which limits the inferences that can be made from these results. For other information-processing biases included in the review, too few studies were identified to make inferences about their relationship with trauma, which highlights the paucity of research in this area.

8.1.3 Study III: Childhood trauma, abnormal belief-updating processes, and psychotic experiences

8.1.3.1 Abnormal belief-updating processes and PEs

In study III, I investigated whether there is an association between abnormal belief-updating processes and an increased likelihood of PEs using indices of belief-updating derived from performance on two probabilistic inference tasks (the DTD task and the probability estimation task). I found evidence of an association between abnormal belief-updating processes and PEs. Specifically, individuals with an increased likelihood of PEs show increased decision noise and expectation of reversal; these associations were not explained by potential sources of confounding (cognitive functioning, indices of socio-economic status and genetic risk of schizophrenia) and are in line with previous studies in clinical populations (Adams et al., 2018; Moutoussis et al., 2011).

My results also suggest that there is an absence of an association other belief-updating processes, as measured by several computational indices, and PEs. In the DTD task, I did not find evidence to suggest that people with PEs estimate the cost of requesting additional beads (cost of sampling) to be greater when completing the task. This finding suggests that people with PEs or psychotic disorder are unlikely to be using a consistent strategy in the DTD task that favours drawing fewer beads due to reasoning or motivational factors. Despite previous findings that people with psychosis-related symptoms have reported lower confidence in their estimations when completing the beads task (Klein and Pinkham, 2018; McKay et al., 2007; Moritz et al., 2016), there was little evidence to support an association between decision confidence in the probability estimation task and PEs. There was also a lack of support for the view that PEs are associated with how much previous information is used to update an estimation (inference window; FitzGerald, Hämmerer, Friston, Li, & Dolan, 2017) or how estimations are adjusted in response to new information (adjustment rate; Adams et al., 2018; Stuke, Stuke, Weilnhammer, & Schmack, 201). Based on the sample size of the study, which is substantially larger than previous studies to date, findings of a lack of effect are unlikely to be due to low statistical power.

I also investigated whether behavioural, rather than computational, indices of abnormal belief-updating (lower average DTD, the JTC bias, increased contrary updating) are associated with PEs. As discussed in the previous chapter, the information provided from these indices is limited as they do not indicate what underlying processes may contribute to altered belief-updating (e.g. motivational factors, differences in reasoning methods). As behavioural indices have been studied extensively in previous literature, this analysis aimed to allow comparison with previous studies that have reported mixed evidence of an association between behavioural indices and psychosis-related outcomes (Dudley et al., 2015;

Klein & Pinkham, 2018). By contrast to what has been previously found in some general population samples, my results did not suggest that there is an association between behavioural indices of abnormal belief-updating and an increased likelihood of psychosis-related outcomes (Balzan, Delfabbro, Galletly, & Woodward, 2012; Ross et al., 2016). My finding may suggest that studies that do report an association between the JTC bias and PEs may be subject to bias or that the JTC bias may not be a reliable measure of abnormal belief-updating processes associated with PEs.

Meta-cognitive therapy, a form of psychotherapy, targets information-processing biases and has been used to reduce psychotic symptoms in clinical samples (Hutton et al., 2014). While there is evidence that meta-cognitive therapy can reduce psychotic symptoms, there are mixed findings as to whether this intervention also reduces the likelihood of the JTC bias (Garety et al., 2015; Gawęda, Krężołek, Olbryś, Turska, & Kokoszka, 2015; Pos et al., 2018; Ross, Freeman, Dunn, & Garety, 2011). The lack of consistent evidence of a relationship between symptom decline and a reduction of the JTC bias may be due to the use of an index that does not measure specific processes of belief-updating. Based on findings from computational analyses of the beads task in study III and previous studies, computational modelling of performance on probabilistic inference tasks have the potential to provide evidence of specific abnormal belief-updating processes associated with symptom improvement that could inform meta-cognitive interventions.

To assess the claim that abnormal belief-updating processes are specifically associated with delusions (Bentall et al., 2012; Freeman & Garety, 2014), I examined whether abnormal belief-updating processes are differentially associated with sub-clinical hallucinations and delusions. Results from a bivariate analysis suggest that there is little evidence to support a differential association between any of the indices of abnormal belief-updating analysed and hallucinations or delusions. This finding indicates that there may be shared processes that contribute to different psychotic outcomes.

Another aim in study III was to examine whether abnormal belief-updating processes were specific to an increased risk of PEs or if they were also associated with an increased risk of non-psychotic psychopathology (anxiety or depression). Based on results from the multivariate analysis of depression, anxiety and PEs, there was little evidence to suggest that an increased expectation of change or greater decision noise is associated with a greater likelihood of symptoms of anxiety or depression, which suggest that these abnormal belief-updating processes are specific to PEs. Recent studies have proposed that impaired predictive processing for positive or negative events may increase the risk of anxiety and depression (Kube et al., 2019; Pulcu & Browning, 2017). My findings may inform these models by providing evidence that suggests abnormal belief-updating processes are not likely to be associated with symptoms of anxiety or depression when inferring the likelihood of an event using neutral stimuli (coloured beads).

8.1.3.2 Exposure to trauma and abnormal belief-updating processes

Results from study III suggest that exposure to trauma is associated with greater decision noise; an index of the extent to which participants are employing an unmodelled sub-optimal belief-updating strategy or are responding inconsistently in the task. My results suggest that the effect of trauma on increased decision noise is independent of socio-demographic differences or cognitive functioning. The finding that the strength of this effect increased as the number of trauma types reported increased, in a dose-response manner, also suggests that this relationship is likely to be causal. In line with a previous study, I did not find evidence of an association between exposure to childhood trauma and a greater likelihood of the JTC bias (Freeman et al., 2008).

My finding of an association between childhood trauma and sub-optimal belief-updating (decision noise) is in line with findings from previous studies, using different decision-making tasks, that suggest childhood trauma is associated with both poorer decision-making and a blunted response to reward-related stimuli (Birn et al., 2017; Dillon et al., 2009; Eckstrand et al., 2019). Furthermore, sub-optimal performance on decision-making tasks is likely to have a neural basis and be indicative of the adverse impact of childhood trauma on brain development (Carrion & Wong, 2012; Cassiers et al., 2018).

8.1.3.3 Mediation analysis of trauma, belief-updating processes and psychotic experiences

The final aim of study III was to investigate if abnormal belief-updating processes mediate the relationship between exposure to trauma and subsequent PEs. As there was evidence from my earlier analysis that increased decision noise in the DTD task was associated with both prior exposure to trauma and increased risk of PEs, I selected decision noise (DTD task) as a candidate variable to test in a mediation model. Inconsistent with my hypothesis, I did not find evidence that abnormal belief-updating processes mediate the relationship between exposure to trauma and an increased risk of PEs. However, these findings are limited by decision noise being an index of an unmodelled, sub-optimal or inconsistent belief-updating process rather than a distinct belief-updating process; there may be specific processes that do mediate this pathway that are not captured by the current computational models used.

8.2 Limitations

As discussed previously, observational studies are more vulnerable to biases that may undermine the validity of observed causal effects compared to the 'gold standard' randomised control trial study design. A trial-based study design to examine outcomes of trauma exposure is not possible due to ethical reasons; therefore, research in the area is limited to observational studies. Throughout the thesis, I have considered the potential influence of non-causal sources of association (e.g. confounding, selection bias, reverse causation, measurement error) on my findings and the extent to which previous studies have addressed these limitations.

8.2.1 Confounding

As discussed in Chapter 1, several cohort studies had adjusted for some confounders (e.g. education, family history of psychosis; Arseneault et al., 2011; De Loore et al., 2007); however, these studies had not adjusted for multiple confounders in a single model and it was unclear whether the relationship between trauma and PEs is explained by residual confounding. On the other hand, some studies had also adjusted for variables that are likely to mediate the association between trauma and PLEs or PEs (e.g. drug use, stress in adulthood; Abajobir et al., 2017; Wigman et al., 2011) and are likely to have underestimated the effect of trauma on the risk of psychosis-related outcomes. There were also potential confounders in the relationship between trauma and PEs (childhood temperament, developmental delay, genetic risk for non-psychotic psychopathology; Algood, Hong, Gourdine, & Williams, 2011; Brown, Cohen, Johnson, & Salzinger, 1998) that had not been, to my knowledge, previously investigated.

To address these limitations of study I, I identified a range of variables in the ALSPAC cohort to test as confounders in my analysis of trauma and PEs. I tested each selected confounder individually and only included those that attenuated the unadjusted effect in the complete-case sample by 5% or more. This approach was taken as including a large amount of confounders would increase missing data and an increase in standard error in regression analysis. Furthermore, including a smaller number of confounders in the imputation model reduces the complexity of the model to predict missing values. However, testing selected confounders may have resulted in residual confounding and an overestimation of the effect of trauma on PEs. Overall, adjusting for confounding did not substantially attenuate unadjusted estimated effect size in study I; therefore, it is unlikely that the association between trauma and PEs is accounted for by residual confounding.

For study II, I reviewed the role of confounding in the relationship between exposure to trauma and information-processing biases in my quality assessment of included studies. Very few studies (8%) included in the systematic review had adjusted for variables such as cognitive functioning and socio-economic status that I identified as potentially important confounders. As a result, it is difficult to conclude that these factors do not account for the observed associations in my results.

In study III, I also found that my observed associations between (i) abnormal belief-updating processes and PEs and (ii) trauma and abnormal belief-updating processes were unlikely to be explained by potential sources of confounding (e.g. cognitive processing, socio-economic status and genetic risk for schizophrenia). However, it is impossible to exclude residual confounding.

8.2.2 Reverse Causality

As discussed in Chapter 1, it is unlikely that the association between exposure to childhood trauma in early childhood (age 0-5 years) and PEs is due to reverse causality because the onset of PEs occurs later in development and would temporally follow trauma exposure. Results from a sensitivity analysis restricting the sample to those who did not report PEs at age 12 years supports the hypothesis that the observed relationship is not due to reverse causality. The finding of a lack of evidence to support reverse causality is in line with a previous study that also excluded participants with PLEs at baseline and reported an association between trauma and an increased risk of subsequent PLEs (Lataster et al., 2012).

In study III, a key limitation of my analysis of the relationship between abnormal belief-updating processes and the likelihood of PEs is that both the exposure and outcome were assessed at age 24 years. I was unable to rule out the possibility that the observed effects are due to reverse causality and that abnormal belief-updating processes are a consequence of PEs.

I was able to use longitudinal data for my analysis of trauma and abnormal belief-updating, which does reduce the likelihood of reverse causality compared to cross-sectional data. It is unlikely that sub-optimal belief-updating strategies (decision noise) would increase the likelihood of trauma exposure, particularly for exposure during early childhood.

8.2.3 Selection bias

Lower socioeconomic status and poorer educational attainment are associated with greater attrition in cohort studies (Howe et al., 2013). As lower socio-economic status is correlated with trauma exposure (Bell et al., 2019; Fisher et al., 2015), trauma is also likely to be associated with a greater likelihood of attrition. Therefore, longitudinal studies that do not adequately address attrition where it is substantial, for example, through methods such as multiple imputation, may lead to biased estimates of the effect of trauma on psychosis-related outcomes.

Of previous longitudinal studies that have analysed exposure to trauma and the likelihood of PLEs or PEs, some studies have reported the use of sampling probability weighting and multiple imputation to compare the magnitude of effects with analyses in complete-case data (Abajobir et al., 2017; Janssen et al., 2004). However, other studies have only reported results from analyses from complete-case data where the proportion of missing data at follow-up is notable (Bell et al., 2019; Ian Kelleher et al., 2013; Janneke Spauwen et al., 2006; Wigman et al., 2011) or rates of attrition are not reported (De Loore et al., 2007), and therefore results from these may have been affected by selection bias. Arsenault and colleagues (2011) report complete-case analyses of a sample with a low rate of attrition (3.9%), and thus attrition bias is less likely.

For both studies analysing ALSPAC data (studies I and III), I used multiple imputation to predict missing values for incomplete data on trauma exposure and confounding variables. As I used several covariates associated with an increased likelihood of attrition in the imputation model, it is likely that this method does reduce the possible bias from attrition, although it remains possible that bias is affecting the reported results.

For study II, selection bias was a potential source of bias for studies included in the systematic review. The majority of studies included in the search were assessed as lower quality due to low participation rates (<75%) and non-random methods of ascertainment, which means that samples may not have been representative of the target population and introduced selection bias. Selection bias may have also contributed to the high heterogeneity in the meta-analysis, as indexed by the I^2 statistic, which limits what inferences can be made about the pooled estimate from the review.

8.2.4 Measurement Error

8.2.4.1 Trauma Exposure

There are several potential sources of measurement error (Chapter 1) that have been identified in studies of childhood trauma. If the magnitude of measurement error differs for participants according to PEs status (i.e. people with PEs are more or less likely to report trauma exposure compared to those without PEs), the true effect of trauma on the likelihood of PEs may be overestimated or underestimated due to differential measurement error.

Another consideration is whether trauma is reported by the individual, a family member or based on assessments by local authorities. Trauma exposure collected by self-report is more likely to be valid than parent-reported trauma, where parents report lower prevalence of exposure to and underestimate the psychological impact of trauma on their child compared to self-reports from children (Stover et al., 2010). The effects of trauma exposure reported by parents on the risk of PEs has been lower in comparison to child-reported exposure (Arseneault et al., 2011). Furthermore, there is evidence that agreement between self-reported childhood trauma and at a later age-period is lower in studies that used questionnaire assessments compared to interview (Baldwin et al., 2019), which suggests that methods of trauma assessment can contribute to measurement error.

I addressed potential sources of errors using sensitivity analyses to investigate if effects differed according to whether: (i) trauma was reported by parents or children, and (ii) trauma was reported during the age-period of exposure or recalled when asked at age 22 years. Based on results from the sensitivity analyses, it does not appear that the observed estimated effect of exposure to trauma on the risk of PEs differs according to whether data on trauma exposure were collected from parents or children or the timing of trauma assessment, which suggests that the observed effects were not due to measurement error from these sources. However, it is likely that measurement error does contribute to the observed effects to some extent as participants may not be willing to disclose traumatic exposures or not identify their own experiences as traumatic; these errors are likely to be non-differential and lead to an underestimation of effects.

8.2.4.2 PEs

As summarised in Chapter 1, the difference in the prevalence of psychotic experiences according to whether symptoms are rated by a trained interviewer using a semi-structured approach or based on self-report suggests that self-report assessments are more prone to measurement error (Linscott & Os, 2013). A key strength of studies I & III is the use of rater-reported assessments of PEs, which enabled me to address limitations in the majority of previous studies that had used self-report measures of PLEs. However, there is also likely to be some measurement error in the assessment of PEs as participants may not want to disclose symptoms of psychosis to an interviewer due to social desirability biases (DeVylder & Hilimire, 2015) or not recognise their experiences as abnormal. Furthermore, interviewers may be biased in their rating of PEs; for example, a participant who is personable and articulate about their abnormal experiences may be less likely to be rated as having suspected PEs than a participant who is less able to articulate their experiences.

8.2.4.3 Abnormal belief-updating processes

As discussed in the previous chapter, a study of the probability estimation task in a clinical sample reported that the ‘over-adjustment’ bias was accounted for by a lack of comprehension in a clinical sample, with qualitative evidence to suggest that participants who revised their estimations rapidly had misunderstood instructions (Balzan et al., 2012). A limitation in the current evidence base is that other studies have not been able to rule out the influence of task comprehension on their results of the relationship between performance on probabilistic inference task and psychosis-related outcomes. In my study, researchers explained the task and delivered a trial run of the task and attempts were made to make sure that participants understood the task.

Study III was the first, to my knowledge, to use a hidden Markov model to fit data from performance on the probability estimation task to infer what abnormal belief-updating processes are associated with psychiatric outcomes (FitzGerald et al., 2017); this means that the validity of these parameters as measures of belief-updating for the probability estimation task has not been established in previous literature. Based on the absence of studies that have examined the reliability of performance at multiple timepoints and the lack of a 'gold-standard' measure to compare performance to, it is likely that there is measurement error in the assessment of abnormal belief-updating processes. If the measurement error is non-differential according to PEs or trauma exposure status, the effects detected in study III may be underestimated. However, the effects may be underestimated or overestimated if the measurement error is differential.

8.3 Implications

As discussed in Chapter 1, exposure to childhood trauma is a major public health concern due to the substantial proportion of the population that are affected and the increased risk of a wide range of negative physical and mental health outcomes. In a recent report by the Young Minds Trust and Health Education England, a priority for improving mental health care is to develop practices that include a common framework to identify exposure to trauma in young people and to develop trauma-informed approaches to mental health treatment (Bush, 2018). In Scotland, public sector workers are being trained to understand the effects of childhood trauma in contexts including criminal justice, education and social work (NHS Education for Scotland, 2017). As PEs are associated with an increased risk of a wide range of negative mental health outcomes (Healy et al., 2019), my findings also suggest that trauma contributes to the development of non-psychotic mental health disorders. Developing the current evidence base for the relationship between exposure to childhood trauma and subsequent PEs and identifying possible mechanisms on this pathway may have implications for mental health care.

8.3.1 Exposure to trauma and PEs

In line with previous PAF estimates (McGrath et al., 2015; Varese et al., 2012), which are based on the assumption that the relationship is causal and estimates are not biased, I found that 45% of individuals in the sample would not have developed PEs if they had not been exposed to childhood trauma.

Results from study I suggest that clinicians, including GPs and secondary care practitioners, should screen individuals with PEs for exposure to childhood trauma and incorporate this information into case formulations and approaches to treatment. Furthermore, clinicians should examine whether PEs are related to traumatic exposure; for example, hallucinations may be intrusive memories from the traumatic event and paranoia may be extreme forms of hyperarousal. Understanding PEs in the context of traumatic experiences and potential manifestation of PTSD symptomatology can help to understand the symptoms and strengthen the rationale for the use of trauma-based interventions.

Current treatments for trauma exposure on mental health outcomes are mainly used for the treatment of post-traumatic stress disorder; a disorder that commonly overlaps with psychotic symptoms. The current NICE guidelines (2018) for treatments of PTSD recommend the use of therapies including trauma-focused cognitive behavioural therapy, narrative exposure therapy and Eye Movement Desensitization and Reprocessing (EMDR). These interventions require individuals to discuss their traumatic experiences with a therapist over a series of sessions to psychologically process these experiences and trauma-related emotions. There is evidence from trial-based studies to support the claim that EMDR and exposure therapy are effective methods to reduce symptoms of PTSD, and possibly also psychotic symptoms, in people with co-morbid psychotic disorder and PTSD (van den Berg et al., 2016; van den Berg & van der Gaag, 2012; van den Berg, de Bont, van der Vleugel & et al., 2015). A meta-analysis of 21 trials shows that trauma-focused CBT is likely to be an effective intervention to reduce symptoms of PTSD and co-occurring depression (Lenz & Hollenbaugh, 2015).

Based on the evidence of a causal role between exposure to trauma and PEs, trauma-focused interventions could be used for people with PEs who have been exposed to multiple types of trauma to reduce the risk of persistent PEs and mental health disorders. In addition to screening individuals with PEs for trauma exposure, professionals who are aware that a young person has been exposed to trauma (e.g. teachers, GPs, social services) should screen them for PEs and refer them to appropriate services if required. The early identification of individuals at high risk of PEs due to trauma exposure can help to prevent long-term harmful outcomes and mitigate the psychological effects of trauma on the risk of psychopathology.

8.3.2 Abnormal belief-updating and PEs

My findings challenge the assumption, made by several studies, that the JTC bias is a reliable measure of a bias associated with PEs; this may also bring into question the association between the JTC bias and psychotic symptoms in clinical populations.

The association between abnormal belief-updating processes and PEs (frequent or distressing PEs in the last six months) may suggest that abnormal-belief updating processes are detectable before the development of more severe psychotic symptoms. If it is established that abnormal belief-updating processes are modifiable, this could be specifically targeted in meta-cognitive treatments to improve symptom outcomes. An increased expectation of change for individuals with psychotic symptoms may also inform approaches to treatment; ensuring that service provision is consistently delivered (e.g. regular scheduling of treatment) may help to reduce an individual’s expectation of change and potentially reduce stress and overall quality of life that may increase the severity or frequency of PEs.

8.3.3 Exposure to trauma and abnormal belief-updating processes

My results suggest that exposure to trauma during childhood and adolescence increases the likelihood of greater decision noise in both the DTD task and probability estimation task at age 24 years in a dose-response manner. If people who are exposed to trauma are more likely to use sub-optimal strategies to infer the likelihood of different outcomes this may contribute to difficulties adapting to environments which, in turn, could lead to negative mental health outcomes.

In a comparable model to the predictive processing account of psychosis, the predictive processing of PTSD suggests that traumatic stress increases expectations of threat and alters the perception of neutral stimuli that are associated with, but unrelated to, the original trauma exposure and lead to symptoms of PTSD (Chamberlin, 2019; Wilkinson et al., 2017). This impaired ability to reality-test information may contribute to my finding of an association between exposure to trauma and decision noise in study III. Abnormal predictive processing from childhood trauma may explain why symptoms of PEs and PTSD commonly overlap. By understanding trauma as a contributing factor for abnormal predictive processing that could increase the likelihood of PEs or PTSD, this may help clinicians to understand psychosis-related outcomes in the context of prior trauma exposure.

If abnormal belief-updating processes can be identified as part of the pathway from trauma to PEs and are modifiable, these processes could be tested as part of a screening, depending on the feasibility and reliability of the cognitive tests, for those at increased risk of PEs from exposure to childhood trauma and complex stressors (e.g. seeking asylum) by front-line professionals. Furthermore, in clinical populations, the identification of these abnormal belief-updating processes could be used to identify targets of intervention to prevent the relapse of symptoms.

8.4 Directions for future study

8.4.1 Understanding the longitudinal association between trauma and PEs

Very few studies have investigated the role of the effects of trauma during sensitive periods in development on the risk of PEs. While my study aimed to tease apart the effects of trauma during different age-periods from an overall dose of trauma during childhood, I did not have data available on the frequency of exposure to different types of trauma during development. Future studies require both data on trauma frequency and statistical methods that can model period-specific effects to help to answer questions about sensitive period effects on PEs risk. While study I examined PEs at a single time-point (age 18 years), further studies can investigate the role of trauma during different age periods on trajectories of PEs (e.g. increasing, intermittent or decreasing PEs) and investigate the effects of short-term and chronic trauma on PEs trajectories and psychosis symptom development.

8.4.2 Potential mechanisms on the pathway from trauma to PEs

Future studies need to investigate belief-updating biases in different tasks (e.g. source monitoring, reversal learning) and, where appropriate, use computational models to advance knowledge of mechanisms on the pathway to psychosis.

Based on my findings from study II, further investigation using longitudinal data is needed to establish whether external LOC is a mechanism on the trauma-PEs pathway. As discussed in Chapter 1, other psychological mechanisms that may be on the pathway from trauma to PEs include a negative worldview towards the self and others (negative cognitive schema), a persistent feeling of marginalisation (social defeat) and poor emotional regulation. Evidence to support the hypothesis that these psychological mechanisms are mediators of trauma and psychosis-related outcomes is mixed (Bak et al., 2005; Hardy, 2017; van Nierop et al., 2014; Williams et al., 2018) and further studies using longitudinal data are needed to elucidate the role of these biases on the pathway to PEs as these could help the development of trauma-informed interventions.

As discussed in chapter 2, the dopamine model of psychosis states that environmental stressors, including traumatic stress, contribute to an increased likelihood of psychosis-related outcomes by dysregulating dopamine activation (Howes & Kapur, 2009) and there is evidence that dopamine dysregulation contributes to the development of psychosis-related outcomes and is triggered in response to trauma (Egerton et al., 2013; Mohr & Ettinger, 2014; Prabhu et al., 2018). Future studies should investigate whether dopamine dysregulation mediates the relationship between exposure to trauma and psychotic outcomes across the psychosis continuum (i.e. in both sub-clinical and clinical contexts) to identify whether targeting dopamine dysregulation at earlier stages of symptom development could prevent the development of psychotic disorder (Howes, McCutcheon, Owen, & Murray, 2017).

There is evidence that exposure to childhood trauma may increase the risk of harmful behaviours, including increased drug use, and exposure to high-risk environments (Mandavia et al., 2016; Thompson et al., 2017). Mediation analyses in cross-sectional study designs have not found evidence to support the hypothesis that cannabis use mediates the association between trauma and PLEs (Bebbington et al., 2011; van Nierop et al., 2014). Further studies are needed to establish the temporal relationship between early trauma, drug misuse and risk-taking behaviours, and the development of PEs and other psychiatric outcomes. These findings would provide greater insight into the psychosis pathway and potential areas of intervention to mitigate the risk of PEs. There is also evidence that other mental health disorders may mediate trauma and psychotic symptoms. In particular, PTSD is a candidate mediator based on the overlap in symptomology, shared aetiological factors, and high co-morbidity between psychosis and PTSD (Choi et al., 2015; Alsawy et al., 2015; Sareen et al., 2005; Hardy, 2017). Further studies may be able to apply these findings to intervention development by using trauma-focused therapies (e.g. EMDR, narrative exposure therapy) or trauma-informed interventions (e.g. compassion-focused therapy) for individuals who have been exposed to trauma and are at increased risk of developing psychosis.

8.4.3 Exposure to trauma, abnormal belief-updating processes and psychotic experiences

Based on my results and previous studies, the JTC bias is unlikely to be a useful index of abnormal belief-updating processes associated with PEs. Furthermore, the use of computational models to derive measures of specific belief-updating processes may be more valuable than behavioural indices for identifying mechanisms on the pathway from trauma to PEs. As my study did not identify specific processes on the trauma-PEs pathway, future studies may benefit from using tasks that are not used in the thesis to examine belief-updating. Based on previous literature of related tasks, tasks that involve processes such as learning from feedback and reversal learning, reward-processing and the attribution of salience may be able to identify specific abnormal processes associated with PEs.

As discussed in Chapter 2, the field of computational psychiatry aims to develop unified models of psychopathology by testing hypotheses about underlying neural and behavioural mechanisms that contribute to different mental health outcomes (Anticevic & Murray, 2017). The conceptualisation of different mental health outcomes according to different characteristics of abnormal predictive processing (e.g. depression, PTSD, psychosis; Griffin & Fletcher, 2017; Kube et al., 2019; Wilkinson, Dodgson, & Meares, 2017) have the potential to be tested empirically to identify distinct and overlapping processes that may contribute to the development of psychopathology. The predictive processing framework of psychopathology could inform how different mental health disorders are conceptualised by informing diagnostic criteria (e.g. Research Domain Criteria; Cuthbert, 2015) and approaches to treatment. In the case of psychosis, my findings suggest that people with psychosis are more likely to respond abnormally to inconsistent information and that this is likely to contribute to abnormalities in information-processing at different levels of an information-processing hierarchy. Further studies are needed to investigate how abnormal responses to contrary information may be manifest in different contexts and whether this process temporally precedes the development of psychotic disorder; these finding would inform models of psychosis and, potentially, intervention strategies.

8.5 Conclusions

The associations between exposure to trauma during childhood and adolescence and subsequent PEs are consistent with the thesis that exposure to trauma is a causal risk factor for the development of PEs. This relationship was not explained by potential sources of confounding and is unlikely to be due to reverse causality, measurement error or selection bias, which are key limitations that I identified in previous studies in the field. I found that exposure to different types of interpersonal violence and neglect during childhood and adolescence are associated with PEs. Exposure to multiple types of trauma was associated with a greater risk of PEs in a dose-response manner. As my findings support the hypothesis that there is a causal association between trauma and PEs, further investigation is needed of mechanisms on this pathway.

Using indices of performance on probabilistic inference tasks derived from computational modelling, I found evidence that people with PEs are more likely to have sub-optimal belief-updating processes (increased decision noise) and a greater expectation that the outcome of an event will change (increased expectation of reversal), although there was little evidence that these mediate the relationship between trauma and PEs. Studies using longitudinal data are needed to infer whether these abnormal belief-updating processes precede the development of PEs and to establish whether these could be target mechanisms in future interventions to prevent the development of psychosis.

References

Abajobir, A. A., Kisely, S., Scott, J. G., Williams, G., Clavarino, A., Strathearn, L., & Najman, J. M. (2017). Childhood Maltreatment and Young Adulthood Hallucinations, Delusional Experiences, and Psychosis: A Longitudinal Study. *Schizophrenia Bulletin*, *43*(5), 1045–1055. https://doi.org/10.1093/schbul/sbw175

Aboraya, A., Tien, A., Stevenson, J., & Crosby, K. (1998). Schedules for Clinical Assessment in Neuropsychiatry (SCAN): Introduction to WV's mental health community. *The West Virginia Medical Journal*, *94*(6), 326–328.

Adams, R. A., Napier, G., Roiser, J. P., Mathys, C., & Gilleen, J. (2018). Attractor-like dynamics in belief updating in schizophrenia. *Journal of Neuroscience*, 3163–17. https://doi.org/10.1523/JNEUROSCI.3163-17.2018

Alastalo, H., Raikkonen, K., Pesonen, A.-K., Osmond, C., Barker, D. J. P., Kajantie, E., Heinonen, K., Forsen, T. J., & Eriksson, J. G. (2009). Cardiovascular health of Finnish war evacuees 60 years later. *Annals of Medicine*, *41*(1), 66–72. https://doi.org/10.1080/07853890802301983

Aleman, A. (2014). Neurocognitive Basis of Schizophrenia: Information Processing Abnormalities and Clues for Treatment. *Advances in Neuroscience*, *2014*, e104920. https://doi.org/10.1155/2014/104920

Algood, C. L., Hong, J. S., Gourdine, R. M., & Williams, A. B. (2011). Maltreatment of children with developmental disabilities: An ecological systems analysis. *Children and Youth Services Review*, *33*(7), 1142–1148. https://doi.org/10.1016/j.childyouth.2011.02.003

Alisic, E., Zalta, A. K., Wesel, F. van, Larsen, S. E., Hafstad, G. S., Hassanpour, K., & Smid, G. E. (2014). Rates of post-traumatic stress disorder in trauma-exposed children and adolescents: Meta-analysis. *The British Journal of Psychiatry*, *204*(5), 335–340. https://doi.org/10.1192/bjp.bp.113.131227

Allswede, D. M., & Cannon, T. D. (2018). Prenatal inflammation and risk for schizophrenia: A role for immune proteins in neurodevelopment. *Development and Psychopathology*, *30*(3), 1157–1178. https://doi.org/10.1017/S0954579418000317

Alsawy, S., Wood, L., Taylor, P. J., & Morrison, A. P. (2015). Psychotic experiences and PTSD: Exploring associations in a population survey. *Psychological Medicine*, *45*(13), 2849–2859. https://doi.org/10.1017/S003329171500080X

An, S. K., Kang, J. I., Park, J. Y., Kim, K. R., Lee, S. Y., & Lee, E. (2010). Attribution bias in ultra-high risk for psychosis and first-episode schizophrenia. *Schizophrenia Research*, *118*(1), 54–61. https://doi.org/10.1016/j.schres.2010.01.025

Andersen, S. L., & Teicher, M. H. (2008). Stress, sensitive periods and maturational events in adolescent depression. *Trends in Neurosciences*, *31*(4), 183–191. https://doi.org/10.1016/j.tins.2008.01.004

Andreou, C., Moritz, S., Veith, K., Veckenstedt, R., & Naber, D. (2014). Dopaminergic Modulation of Probabilistic Reasoning and Overconfidence in Errors: A Double-Blind Study. *Schizophrenia Bulletin*, *40*(3), 558–565. https://doi.org/10.1093/schbul/sbt064

Andreou, E. (2000). Bully/victim problems and their association with psychological constructs in 8- to 12-year-old Greek schoolchildren. *Special Issue: Bullying in the Schools.*, *26*(1), 49–56.

Andrews, B., & Brown, G. W. (1988). Marital Violence in the Community: A Biographical Approach. *The British Journal of Psychiatry*, *153*(3), 305–312. https://doi.org/10.1192/bjp.153.3.305

Anticevic, A., & Murray, J. D. (2017). *Computational psychiatry: Mathematical modeling of mental illness*. Academic Press.

Anticevic, A., & Murray, J. D. (2018). *Computational Psychiatry: Mathematical Modelling of Mnetal Illness*. Academic Press.

Appiah-Kusi, E., Fisher, H. L., Petros, N., Wilson, R., Mondelli, V., Garety, P. A., Mcguire, P., & Bhattacharyya, S. (2017). Do cognitive schema mediate the association between childhood trauma and being at ultra-high risk for psychosis? *Journal of Psychiatric Research*, *88*, 89–96. https://doi.org/10.1016/j.jpsychires.2017.01.003

Arseneault, L., Cannon, M., Fisher, H. L., Polanczyk, G., Moffitt, T. E., & Caspi, A. (2011). Childhood Trauma and Children's Emerging Psychotic Symptoms: A Genetically Sensitive Longitudinal Cohort Study. *American Journal of Psychiatry*, *168*(1), 65–72. https://doi.org/10.1176/appi.ajp.2010.10040567

Attademo, L., Bernardini, F., Garinella, R., & Compton, M. T. (2017). Environmental pollution and risk of psychotic disorders: A review of the science to date. *Schizophrenia Research*, *181*, 55–59. https://doi.org/10.1016/j.schres.2016.10.003

Austin, S., & Joseph, S. (1996). Assessment of bully/victim problems in 8 to 11 year-olds. *British Journal of Educational Psychology*, *66*(4), 447–456. https://doi.org/10.1111/j.2044-8279.1996.tb01211.x

Averbeck, B. B., Evans, S., Chouhan, V., Bristow, E., & Shergill, S. S. (2011). Probabilistic learning and inference in schizophrenia. *Schizophrenia Research*, *127*(1), 115–122. https://doi.org/10.1016/j.schres.2010.08.009

Azur, M. J., Stuart, E. A., Frangakis, C., & Leaf, P. J. (2011). Multiple imputation by chained equations: What is it and how does it work? *International Journal of Methods in Psychiatric Research*, *20*(1), 40–49. https://doi.org/10.1002/mpr.329

Bailey, T., Alvarez-Jimenez, M., Garcia-Sanchez, A. M., Hulbert, C., Barlow, E., & Bendall, S. (2018). Childhood Trauma Is Associated With Severity of Hallucinations and Delusions in Psychotic Disorders: A Systematic Review and Meta-Analysis. *Schizophrenia Bulletin*. https://doi.org/10.1093/schbul/sbx161

Bak, M., Krabbendam, L., Janssen, I., de Graaf, R., Vollebergh, W., & van Os, J. (2005). Early trauma may increase the risk for psychotic experiences by impacting on emotional response and perception of control. *Acta Psychiatrica Scandinavica*, *112*(5), 360–366. https://doi.org/10.1111/j.1600-0447.2005.00646.x

Baker, S. C., Konova, A. B., Daw, N. D., & Horga, G. (2019). A distinct inferential mechanism for delusions in schizophrenia. *Brain*, *142*(6), 1797–1812. https://doi.org/10.1093/brain/awz051

Baldwin, J. R., Reuben, A., Newbury, J. B., & Danese, A. (2019). Agreement Between Prospective and Retrospective Measures of Childhood Maltreatment: A Systematic Review and Meta-analysis. *JAMA Psychiatry*. https://doi.org/10.1001/jamapsychiatry.2019.0097

Balzan, R. P., Delfabbro, P. H., Galletly, C. A., & Woodward, T. S. (2012). Over-adjustment or miscomprehension? A re-examination of the jumping to conclusions bias. *The Australian and New Zealand Journal of Psychiatry*, *46*(6), 532–540. https://doi.org/10.1177/0004867411435291

Banyard, V. L., Williams, L. M., & Siegel, J. A. (2001). The Long-Term Mental Health Consequences of Child Sexual Abuse: An Exploratory Study of the Impact of Multiple Traumas in a Sample of Women. *Journal of Traumatic Stress*, *14*(4), 697–715. https://doi.org/10.1023/A:1013085904337

Barahal, R. M., Waterman, J., & Martin, H. P. (1981). The social cognitive development of abused children. *Journal of Consulting and Clinical Psychology*, *49*(4), 508–516. https://doi.org/10.1037/0022-006X.49.4.508

Barch, D. M., Carter, C. S., Gold, J. M., Johnson, S. L., Kring, A. M., MacDonald, A. W., Pizzagalli, D. A., Ragland, J. D., Silverstein, S. M., & Strauss, M. E. (2017). Explicit and implicit reinforcement learning across the psychosis spectrum. *Journal of Abnormal Psychology*, *126*(5), 694–711. https://doi.org/10.1037/abn0000259

Barnett, J. H., McDougall, F., Xu, M. K., Croudace, T. J., Richards, M., & Jones, P. B. (2012). Childhood cognitive function and adult psychopathology: Associations with psychotic and non-psychotic symptoms in the general population. *The British Journal of Psychiatry*, *201*(2), 124–130. https://doi.org/10.1192/bjp.bp.111.102053

Baron, R. M., & Kenny, D. A. (1986). The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology*, 1173–1182.

Baumeister, D., Akhtar, R., Ciufolini, S., Pariante, C. M., & Mondelli, V. (2016). Childhood trauma and adulthood inflammation: A meta-analysis of peripheral C-reactive protein, interleukin-6 and tumour necrosis factor-α. *Molecular Psychiatry*, *21*(5), 642–649. https://doi.org/10.1038/mp.2015.67

Bebbington, P. E., Bhugra, D., Brugha, T., Singleton, N., Farrell, M., Jenkins, R., Lewis, G., & Meltzer, H. (2004). Psychosis, victimisation and childhood disadvantage. *The British Journal of Psychiatry*, *185*(3), 220–226. https://doi.org/10.1192/bjp.185.3.220

Bebbington, P., Jonas, S., Kuipers, E., King, M., Cooper, C., Brugha, T., Meltzer, H., McManus, S., & Jenkins, R. (2011). Childhood sexual abuse and psychosis: Data from a cross-sectional national psychiatric survey in England. *The British Journal of Psychiatry*, *199*(1), 29–37. https://doi.org/10.1192/bjp.bp.110.083642

Beck-sander, A. (1995). Childhood Abuse in Adult Offenders: The Role of Control in Perpetuating Cycles of Abuse. *The Journal of Forensic Psychiatry*, *6*(3), 486–498. https://doi.org/10.1080/09585189508410778

Beese, A. G., & Stratton, P. (2004). Causal attributions in delusional thinking: An investigation using qualitative methods. *British Journal of Clinical Psychology*, *43*(3), 267–283. https://doi.org/10.1348/0144665031752961

Belbasis, L., Köhler, C. A., Stefanis, N., Stubbs, B., Os, J. van, Vieta, E., Seeman, M. V., Arango, C., Carvalho, A. F., & Evangelou, E. (2018). Risk factors and peripheral biomarkers for schizophrenia spectrum disorders: An umbrella review of meta-analyses. *Acta Psychiatrica Scandinavica*, *137*(2), 88–97. https://doi.org/10.1111/acps.12847

Bell, C. J., Foulds, J. A., Horwood, L. J., Mulder, R. T., & Boden, J. M. (2019). Childhood abuse and psychotic experiences in adulthood: Findings from a 35-year longitudinal study. *The British Journal of Psychiatry*, 1–6. https://doi.org/10.1192/bjp.2018.264

Bendall, S., Jackson, H. J., & Hulbert, C. A. (2011). What self-generated speech is externally misattributed in psychosis? Testing three cognitive models in a first-episode sample. *Schizophrenia Research*, *129*(1), 36–41. https://doi.org/10.1016/j.schres.2011.03.028

Bentall, R. P., & Fernyhough, C. (2008). Social Predictors of Psychotic Experiences: Specificity and Psychological Mechanisms. *Schizophrenia Bulletin*, *34*(6), 1012–1020. https://doi.org/10.1093/schbul/sbn103

Bentall, R. P., Rowse, G., Shryane, N., Kinderman, P., Howard, R., Blackwood, N., Moore, R., & Corcoran, R. (2009). The cognitive and affective structure of paranoid delusions: A transdiagnostic investigation of patients with schizophrenia spectrum disorders and depression. *Archives of General Psychiatry*, *66*(3), 236–247. https://doi.org/10.1001/archgenpsychiatry.2009.1

Bentall, R. P., Wickham, S., Shevlin, M., & Varese, F. (2012). Do Specific Early-Life Adversities Lead to Specific Symptoms of Psychosis? A Study from the 2007 The Adult Psychiatric Morbidity Survey. *Schizophrenia Bulletin*, *38*(4), 734–740. https://doi.org/10.1093/schbul/sbs049

Bernadyn, T., & Feigenson, K. A. (2018). Data gathering ability contributes to visual organization and probabilistic reasoning. *Heliyon*, *4*(3). https://doi.org/10.1016/j.heliyon.2018.e00582

Bernstein, D. P., Ahluvalia, T., Pogge, D., & Handelsman, L. (1997). Validity of the Childhood Trauma Questionnaire in an adolescent psychiatric population. *Journal of the American Academy of Child and Adolescent Psychiatry*, *36*(3), 340–348. https://doi.org/10.1097/00004583-199703000-00012

Berridge, K. C. (2012). From prediction error to incentive salience: Mesolimbic computation of reward motivation. *The European Journal of Neuroscience*, *35*(7), 1124–1143. https://doi.org/10.1111/j.1460-9568.2012.07990.x

Betancourt, T. S., Newnham, E. A., Birman, D., Lee, R., Ellis, B. H., & Layne, C. M. (2017). Comparing Trauma Exposure, Mental Health Needs, and Service Utilization across Clinical Samples of Refugee, Immigrant, and U.S.-Origin Children. *Journal of Traumatic Stress*, *30*(3), 209–218. https://doi.org/10.1002/jts.22186

Bevan Jones, R., Thapar, A., Lewis, G., & Zammit, S. (2012). The association between early autistic traits and psychotic experiences in adolescence. *Schizophrenia Research*, *135*(1–3), 164–169. https://doi.org/10.1016/j.schres.2011.11.037

Birchwood, M. (2003). Pathways to emotional dysfunction in first-episode psychosis. *The British Journal of Psychiatry*, *182*(5), 373–375. https://doi.org/10.1192/bjp.182.5.373

Birn, R. M., Roeber, B. J., & Pollak, S. D. (2017). Early childhood stress exposure, reward pathways, and adult decision making. *Proceedings of the National Academy of Sciences*, *114*(51), 13549–13554. https://doi.org/10.1073/pnas.1708791114

Björkqvist, K. (2001). Social defeat as a stressor in humans. *Physiology & Behavior*, *73*(3), 435–442.

Bloomfield, M. A. P., Mouchlianitis, E., Morgan, C. J. A., Freeman, T. P., Curran, H. V., Roiser, J. P., & Howes, O. D. (2016). Salience attribution and its relationship to cannabis-induced psychotic symptoms. *Psychological Medicine*, *46*(16), 3383–3395. https://doi.org/10.1017/S0033291716002051

Boehme, R., Deserno, L., Gleich, T., Katthagen, T., Pankow, A., Behr, J., Buchert, R., Roiser, J. P., Heinz, A., & Schlagenhauf, F. (2015). Aberrant Salience Is Related to Reduced Reinforcement Learning Signals and Elevated Dopamine Synthesis Capacity in Healthy Adults. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *35*(28), 10103–10111. https://doi.org/10.1523/JNEUROSCI.0805-15.2015

Bora, E., Yücel, M., & Pantelis, C. (2010). Cognitive Impairment in Affective Psychoses: A Meta-analysis. *Schizophrenia Bulletin*, *36*(1), 112–125. https://doi.org/10.1093/schbul/sbp093

Bourque, F., Ven, E. van der, & Malla, A. (2011). A meta-analysis of the risk for psychotic disorders among first- and second-generation immigrants. *Psychological Medicine*, *41*(5), 897–910. https://doi.org/10.1017/S0033291710001406

Bowers, M. B., & Freedman, D. X. (1966). 'Psychedelic' experiences in acute psychoses. *Archives of General Psychiatry*, *15*(3), 240–248.

Boyd, A., Golding, J., Macleod, J., Lawlor, D. A., Fraser, A., Henderson, J., Molloy, L., Ness, A., Ring, S., & Davey Smith, G. (2013). Cohort Profile: The 'children of the 90s'--the index offspring of the Avon Longitudinal Study of Parents and Children. *International Journal of Epidemiology*, *42*(1), 111–127. https://doi.org/10.1093/ije/dys064

Bratlien, U., Øie, M., Haug, E., Møller, P., Andreassen, O. A., Lien, L., & Melle, I. (2014). Environmental factors during adolescence associated with later development of psychotic disorders – A nested case-control study. *Psychiatry Research*, *215*(3), 579–585. https://doi.org/10.1016/j.psychres.2013.12.048

Brewin, C. R., & Shapiro, D. A. (1984). Beyond locus of control: Attribution of responsibility for positive and negative outcomes. *British Journal of Psychology*, *75*(1), 43–49. https://doi.org/10.1111/j.2044-8295.1984.tb02788.x

Briere, J., Kaltman, S., & Green, B. L. (2008). Accumulated childhood trauma and symptom complexity. *Journal of Traumatic Stress*, *21*(2), 223–226. https://doi.org/10.1002/jts.20317

Bromberg-Martin, E. S., Matsumoto, M., & Hikosaka, O. (2010). Dopamine in motivational control: Rewarding, aversive, and alerting. *Neuron*, *68*(5), 815–834. https://doi.org/10.1016/j.neuron.2010.11.022

Bromet, E. J., Nock, M. K., Saha, S., Lim, C. C. W., Aguilar-Gaxiola, S., Al-Hamzawi, A., Alonso, J., Borges, G., Bruffaerts, R., Degenhardt, L., de Girolamo, G., de Jonge, P., Florescu, S., Gureje, O., Haro, J. M., He, Y., Hu, C., Karam, E. G., Kovess-Masfety, V., … McGrath, J. J. (2017). Association between psychotic experiences and subsequent suicidal thoughts and behaviors: A cross-national analysis from the World Health Organization World Mental Health Surveys. *JAMA Psychiatry*, *74*(11), 1136–1144. https://doi.org/10.1001/jamapsychiatry.2017.2647

Brookwell, M. L., Bentall, R. P., & Varese, F. (2013). Externalizing biases and hallucinations in source-monitoring, self-monitoring and signal detection studies: A meta-analytic review. *Psychological Medicine*, *43*(12), 2465–2475. https://doi.org/10.1017/S0033291712002760

Brown, A. S., & Derkits, E. J. (2010). Prenatal Infection and Schizophrenia: A Review of Epidemiologic and Translational Studies. *American Journal of Psychiatry*, *167*(3), 261–280. https://doi.org/10.1176/appi.ajp.2009.09030361

Brown, J., Cohen, P., Johnson, J. G., & Salzinger, S. (1998). A longitudinal analysis of risk factors for child maltreatment: Findings of a 17-year prospective study of officially recorded and self-reported child abuse and neglect. *Child Abuse & Neglect*, *22*(11), 1065–1078. https://doi.org/10.1016/S0145-2134(98)00087-8

Brown, S. (1997). Excess mortality of schizophrenia: A meta-analysis. *The British Journal of Psychiatry*, *171*(6), 502–508. https://doi.org/10.1192/bjp.171.6.502

Broyd, A., Balzan, R. P., Woodward, T. S., & Allen, P. (2017). Dopamine, cognitive biases and assessment of certainty: A neurocognitive model of delusions. *Clinical Psychology Review*, *54*, 96–106. https://doi.org/10.1016/j.cpr.2017.04.006

Buck, B., Browne, J., Gagen, E. C., & Penn, D. L. (2020). Hostile attribution bias in schizophrenia-spectrum disorders: Narrative review of the literature and persisting questions. *Journal of Mental Health*, *0*(0), 1–18. https://doi.org/10.1080/09638237.2020.1739240

Bush, M. (2018). *Addressing Adversity*. The YoungMinds Trust. https://youngminds.org.uk/media/2715/ym-addressing-adversity-book-web-2.pdf

Calam, R. M., & Slade, P. D. (1989). Sexual experience and eating problems in female undergraduates. *International Journal of Eating Disorders*, *8*(4), 391–397. https://doi.org/10.1002/1098-108X(198907)8:4<391::AID-EAT2260080402>3.0.CO;2-P

Caldwell, C. B., & Gottesman, I. I. (1990). Schizophrenics kill themselves too: A review of risk factors for suicide. *Schizophrenia Bulletin*, *16*(4), 571–589. https://doi.org/10.1093/schbul/16.4.571

Cancel, A., Comte, M., Boutet, C., Schneider, F. C., Rousseau, P.-F., Boukezzi, S., Gay, A., Sigaud, T., Massoubre, C., Berna, F., Zendjidjian, X. Y., Azorin, J.-M., Blin, O., & Fakra, E. (2016). Childhood trauma and emotional processing circuits in schizophrenia: A functional connectivity study. *Schizophrenia Research*, *0*(0). https://doi.org/10.1016/j.schres.2016.12.003

Carrion, V. G., & Wong, S. S. (2012). Can Traumatic Stress Alter the Brain? Understanding the Implications of Early Trauma on Brain Development and Learning. *Journal of Adolescent Health*, *51*(2, Supplement), S23–S28. https://doi.org/10.1016/j.jadohealth.2012.04.010

Cassiers, L. L. M., Sabbe, B. G. C., Schmaal, L., Veltman, D. J., Penninx, B. W. J. H., & Van Den Eede, F. (2018). Structural and Functional Brain Abnormalities Associated With Exposure to Different Childhood Trauma Subtypes: A Systematic Review of Neuroimaging Findings. *Frontiers in Psychiatry*, *9*. https://doi.org/10.3389/fpsyt.2018.00329

Castelnovo, A., Cavallotti, S., Gambini, O., & D'Agostino, A. (2015). Post-bereavement hallucinatory experiences: A critical overview of population and clinical studies. *Journal of Affective Disorders*, *186*, 266–274. https://doi.org/10.1016/j.jad.2015.07.032

Chaffin, M., Kelleher, K., & Hollenberg, J. (1996). Onset of physical abuse and neglect: Psychiatric, substance abuse, and social risk factors from prospective community data. *Child Abuse & Neglect*, *20*(3), 191–203. https://doi.org/10.1016/s0145-2134(95)00144-1

Chamberlin, D. E. (2019). The Predictive Processing Model of EMDR. *Frontiers in Psychology*, *10*. https://doi.org/10.3389/fpsyg.2019.02267

Chase, K. A., Melbourne, J. K., Rosen, C., McCarthy-Jones, S., Jones, N., Feiner, B. M., & Sharma, R. P. (2019). Traumagenics: At the intersect of childhood trauma, immunity and psychosis. *Psychiatry Research*, *273*, 369–377. https://doi.org/10.1016/j.psychres.2018.12.097

Chen, E., Hanson, M. D., Paterson, L. Q., Griffin, M. J., Walker, H. A., & Miller, G. E. (2006). Socioeconomic status and inflammatory processes in childhood asthma: The role of psychological stress. *The Journal of Allergy and Clinical Immunology*, *117*(5), 1014–1020. https://doi.org/10.1016/j.jaci.2006.01.036

Chiu, C.-D., Tseng, M.-C. M., Chien, Y.-L., Liao, S.-C., Liu, C.-M., Yeh, Y.-Y., & Hwu, H.-G. (2016). Misattributing the Source of Self-Generated Representations Related to Dissociative and Psychotic Symptoms. *Frontiers in Psychology*, *7*, 541.

Choi, J. Y., Choi, Y. M., Kim, B., Lee, D. W., Gim, M. S., & Park, S. H. (2015). The effects of childhood abuse on self-reported psychotic symptoms in severe mental illness: Mediating effects of posttraumatic stress symptoms. *Psychiatry Research*, *229*(1–2), 389–393. https://doi.org/10.1016/j.psychres.2015.05.112

Cicchetti, D., Rogosch, F. A., Gunnar, M. R., & Toth, S. L. (2010). The differential impacts of early physical and sexual abuse and internalizing problems on daytime cortisol rhythm in school-aged children. *Child Development*, *81*(1), 252–269. https://doi.org/10.1111/j.1467-8624.2009.01393.x

Clark, A. (2013). Whatever next? Predictive brains, situated agents, and the future of cognitive science. *Behavioral and Brain Sciences*, *36*(3), 181–204. https://doi.org/10.1017/S0140525X12000477

Cobb-Clark, D. A. (2015). Locus of control and the labor market. *IZA Journal of Labor Economics*, *4*(1), 3. https://doi.org/10.1186/s40172-014-0017-x

Coid, J. W., Hu, J., Kallis, C., Ping, Y., Zhang, J., Hu, Y., Zhang, T., Gonzalez, R., Ullrich, S., Jones, P. B., & Kirkbride, J. B. (2018). Urban Birth, Urban Living, and Work Migrancy: Differential Effects on Psychotic Experiences Among Young Chinese Men. *Schizophrenia Bulletin*, *44*(5), 1123–1132. https://doi.org/10.1093/schbul/sbx152

Colbert, S. M., & Peters, E. R. (2002). Need for closure and jumping-to-conclusions in delusion-prone individuals. *The Journal of Nervous and Mental Disease*, *190*(1), 27–31.

Copeland, W. E., Shanahan, L., Hinesley, J., Chan, R. F., Aberg, K. A., Fairbank, J. A., Oord, E. J. C. G. van den, & Costello, E. J. (2018). Association of Childhood Trauma Exposure With Adult Psychiatric

Disorders and Functional Outcomes. *JAMA Network Open*, *1*(7), e184493–e184493. https://doi.org/10.1001/jamanetworkopen.2018.4493

Corsi-Zuelli, F., Loureiro, C. M., Shuhama, R., Fachim, H. A., Menezes, P. R., Louzada-Junior, P., Mondelli, V., & Del-Ben, C. M. (2019). Cytokine profile in first-episode psychosis, unaffected siblings and community-based controls: The effects of familial liability and childhood maltreatment. *Psychological Medicine*, 1–9. https://doi.org/10.1017/S0033291719001016

Crush, E., Arseneault, L., Jaffee, S. R., Danese, A., & Fisher, H. L. (2018). Protective Factors for Psychotic Symptoms Among Poly-victimized Children. *Schizophrenia Bulletin*, *44*(3), 691–700. https://doi.org/10.1093/schbul/sbx111

Cunningham, T., Hoy, K., & Shannon, C. (2016). Does childhood bullying lead to the development of psychotic symptoms? A meta-analysis and review of prospective studies. *Psychosis*, *8*(1), 48–59. https://doi.org/10.1080/17522439.2015.1053969

Cutajar, M. C., Mullen, P. E., Ogloff, J. R. P., Thomas, S. D., Wells, D. L., & Spataro, J. (2010). Schizophrenia and other psychotic disorders in a cohort of sexually abused children. *Archives of General Psychiatry*, *67*(11), 1114–1119. https://doi.org/10.1001/archgenpsychiatry.2010.147

Cuthbert, B. N. (2015). Research Domain Criteria: Toward future psychiatric nosologies. *Dialogues in Clinical Neuroscience*, *17*(1), 89–97.

da Silva Ferreira, G. C., Crippa, J. A. S., & de Lima Osório, F. (2014). Facial emotion processing and recognition among maltreated children: A systematic literature review. *Frontiers in Psychology*, *5*. https://doi.org/10.3389/fpsyg.2014.01460

Daalman, K., Verkooijen, S., Derks, E. M., Aleman, A., & Sommer, I. E. C. (2012). The influence of semantic top-down processing in auditory verbal hallucinations. *Schizophrenia Research*, *139*(1–3), 82–86. https://doi.org/10.1016/j.schres.2012.06.005

Dale, J., Russell, R., & Wolke, D. (2014). Intervening in primary care against childhood bullying: An increasingly pressing public health need. *Journal of the Royal Society of Medicine*, *107*(6), 219–223. https://doi.org/10.1177/0141076814525071

Dam, D. S. van, Nierop, M. van, Viechtbauer, W., Velthorst, E., Winkel, R. van, Bruggeman, R., Cahn, W., Haan, L. de, Kahn, R. S., Meijer, C. J., Myin-Germeys, I., Os, J. van, & Wiersma, D. (2015). Childhood abuse and neglect in relation to the presence and persistence of psychotic and depressive symptomatology. *Psychological Medicine*, *45*(7), 1363–1377. https://doi.org/10.1017/S0033291714001561

Dam, D. S. van, Ven, E. van der, Velthorst, E., Selten, J. P., Morgan, C., & Haan, L. de. (2012). Childhood bullying and the association with psychosis in non-clinical and clinical samples: A review and meta-analysis. *Psychological Medicine*, *42*(12), 2463–2474. https://doi.org/10.1017/S0033291712000360

Davies, J., Sullivan, S., & Zammit, S. (2018). Adverse life outcomes associated with adolescent psychotic experiences and depressive symptoms. *Social Psychiatry and Psychiatric Epidemiology*, *53*(5), 497–507. https://doi.org/10.1007/s00127-018-1496-z

Davis, K. L., Kahn, R. S., Ko, G., & Davidson, M. (1991). Dopamine in schizophrenia: A review and reconceptualization. *The American Journal of Psychiatry*, *148*(11), 1474–1486. https://doi.org/10.1176/ajp.148.11.1474

De La Rue, L., Polanin, J. R., Espelage, D. L., & Pigott, T. D. (2017). A Meta-Analysis of School-Based Interventions Aimed to Prevent or Reduce Violence in Teen Dating Relationships. *Review of Educational Research*, *87*(1), 7–34. https://doi.org/10.3102/0034654316632061

De Loore, E., Drukker, M., Gunther, N., Feron, F., Deboutte, D., Sabbe, B., Mengelers, R., Os, J. V., & Myin-Germeys, I. (2007). Childhood negative experiences and subclinical psychosis in adolescence: A longitudinal general population study. *Early Intervention in Psychiatry*, *1*(2), 201–207. https://doi.org/10.1111/j.1751-7893.2007.00027.x

DeRosse, P., & Karlsgodt, K. H. (2015). Examining the Psychosis Continuum. *Current Behavioral Neuroscience Reports*, *2*(2), 80–89. https://doi.org/10.1007/s40473-015-0040-7

DeVylder, J. E., & Hilimire, M. R. (2015). Screening for psychotic experiences: Social desirability biases in a non-clinical sample. *Early Intervention in Psychiatry*, *9*(4), 331–334. https://doi.org/10.1111/eip.12161

Dickson, H., Laurens, K. R., Cullen, A. E., & Hodgins, S. (2012). Meta-analyses of cognitive and motor function in youth aged 16 years and younger who subsequently develop schizophrenia. *Psychological Medicine*, *42*(04), 743–755. https://doi.org/10.1017/S0033291711001693

Dillon, D. G., Holmes, A. J., Birk, J. L., Brooks, N., Lyons-Ruth, K., & Pizzagalli, D. A. (2009). Childhood Adversity Is Associated with Left Basal Ganglia Dysfunction During Reward Anticipation in Adulthood. *Biological Psychiatry*, *66*(3), 206–213. https://doi.org/10.1016/j.biopsych.2009.02.019

Dominguez, M. D. G., Wichers, M., Lieb, R., Wittchen, H.-U., & van Os, J. (2011). Evidence That Onset of Clinical Psychosis Is an Outcome of Progressively More Persistent Subclinical Psychotic Experiences: An 8-Year Cohort Study. *Schizophrenia Bulletin*, *37*(1), 84–93. https://doi.org/10.1093/schbul/sbp022

Dorrington, S., Zammit, S., Asher, L., Evans, J., Heron, J., & Lewis, G. (2014). Perinatal maternal life events and psychotic experiences in children at twelve years in a birth cohort study. *Schizophrenia Research*, *152*(1), 158–163. https://doi.org/10.1016/j.schres.2013.11.006

Dreier, J. W., Berg-Beckhoff, G., Andersen, A. M. N., Susser, E., Nordentoft, M., & Strandberg-Larsen, K. (2018). Fever and infections during pregnancy and psychosis-like experiences in the offspring at age 11. A prospective study within the Danish National Birth Cohort. *Psychological Medicine*, *48*(3), 426–436. https://doi.org/10.1017/S0033291717001805

Duan, J., Cheng, Q., Luo, X., Bai, L., Zhang, H., Wang, S., Xu, Z., Gao, J., Zhang, Y., & Su, H. (2018). Is the serious ambient air pollution associated with increased admissions for schizophrenia? *The Science of the Total Environment*, *644*, 14–19. https://doi.org/10.1016/j.scitotenv.2018.06.218

Dudley, R., Daley, K., Nicholson, M., Shaftoe, D., Spencer, H., Cavanagh, K., & Freeston, M. (2013). 'Jumping to conclusions' in first-episode psychosis: A longitudinal study. *British Journal of Clinical Psychology*, *52*(4), 380–393. https://doi.org/10.1111/bjc.12023

Dudley, R., Taylor, P., Wickham, S., & Hutton, P. (2015). Psychosis, delusions and the "jumping to conclusions" reasoning bias: A systematic review and meta-analysis. *Schizophrenia Bulletin*, sbv150.

Dunn, E. C., Crawford, K. M., Soare, T. W., Button, K. S., Raffeld, M. R., Smith, A. D. A. C., Penton-Voak, I. S., & Munafò, M. R. (2018). Exposure to childhood adversity and deficits in emotion recognition: Results from a large, population-based sample. *Journal of Child Psychology and Psychiatry*, *59*(8), 845–854. https://doi.org/10.1111/jcpp.12881

Dunn, E. C., Nishimi, K., Gomez, S. H., Powers, A., & Bradley, B. (2018). Developmental timing of trauma exposure and emotion dysregulation in adulthood: Are there sensitive periods when trauma is most harmful? *Journal of Affective Disorders*, *227*, 869–877. https://doi.org/10.1016/j.jad.2017.10.045

Dykxhoorn, J., Hollander, A.-C., Lewis, G., Magnusson, C., Dalman, C., & Kirkbride, J. B. (2018). Risk of schizophrenia, schizoaffective, and bipolar disorders by migrant status, region of origin, and age-at-migration: A national cohort study of 1.8 million people. *Psychological Medicine*, 1–10. https://doi.org/10.1017/S0033291718003227

Eckstrand, K. L., Hanford, L. C., Bertocci, M. A., Chase, H. W., Greenberg, T., Lockovich, J., Stiffler, R., Aslam, H. A., Graur, S., Bebko, G., Forbes, E. E., & Phillips, M. L. (2019). Trauma-associated anterior cingulate connectivity during reward learning predicts affective and anxiety states in young adults. *Psychological Medicine*, *49*(11), 1831–1840. https://doi.org/10.1017/S0033291718002520

Edwards, D. (2018). Childhood Sexual Abuse and Brain Development: A Discussion of Associated Structural Changes and Negative Psychological Outcomes. *Child Abuse Review*, *27*(3), 198–208. https://doi.org/10.1002/car.2514

Egerton, A., Chaddock, C. A., Winton-Brown, T. T., Bloomfield, M. A. P., Bhattacharyya, S., Allen, P., McGuire, P. K., & Howes, O. D. (2013). Presynaptic striatal dopamine dysfunction in people at ultra-high risk for psychosis: Findings in a second cohort. *Biological Psychiatry*, *74*(2), 106–112. https://doi.org/10.1016/j.biopsych.2012.11.017

Egger, M., Smith, G. D., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ*, *315*(7109), 629–634. https://doi.org/10.1136/bmj.315.7109.629

Ermakova, A. O., Gileadi, N., Knolle, F., Diaz, A. J., Anderson, R., Fletcher, P. C., Moutoussis, M., & Murray, G. (2017). Cost evaluation during decision making in patients at early stages of psychosis. *BioRxiv*, 225920. https://doi.org/10.1101/225920

Ermakova, A. O., Ramachandra, P., Corlett, P. R., Fletcher, P. C., & Murray, G. K. (2014). Effects of methamphetamine administration on information gathering during probabilistic reasoning in healthy humans. *PloS One*, *9*(7), e102683. https://doi.org/10.1371/journal.pone.0102683

Falcone, M. A., Murray, R. M., Wiffen, B. D. R., O'Connor, J. A., Russo, M., Kolliakou, A., Stilo, S., Taylor, H., Gardner-Sood, P., Paparelli, A., Jichi, F., Di Forti, M., David, A. S., Freeman, D., & Jolley, S. (2015). Jumping to conclusions, neuropsychological functioning, and delusional beliefs in first episode psychosis. *Schizophrenia Bulletin*, *41*(2), 411–418. https://doi.org/10.1093/schbul/sbu104

Fear, C. F., & Healy, D. (1997). Probabilistic reasoning in obsessive–compulsive and delusional disorders. *Psychological Medicine*, *27*(01), 199–208.

Felitti, V. J., Anda, R. F., Nordenberg, D., Williamson, D. F., Spitz, A. M., Edwards, V., Koss, M. P., & Marks, J. S. (1998). Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) Study. *American Journal of Preventive Medicine*, *14*(4), 245–258.

Fine, C., Gardner, M., Craigie, J., & Gold, I. (2007). Hopping, skipping or jumping to conclusions? Clarifying the role of the JTC bias in delusions. *Cognitive Neuropsychiatry*, *12*(1), 46–77. https://doi.org/10.1080/13546800600750597

Finkelhor, D., Ormrod, R. K., & Turner, H. A. (2009). Lifetime assessment of poly-victimization in a national sample of children and youth. *Child Abuse & Neglect*, *33*(7), 403–411. https://doi.org/10.1016/j.chiabu.2008.09.012

Fisher, H. L., Caspi, A., Poulton, R., Meier, M. H., Houts, R., Harrington, H., Arseneault, L., & Moffitt, T. E. (2013). Specificity of childhood psychotic symptoms for predicting schizophrenia by 38 years of age: A birth cohort study. *Psychological Medicine*, *43*(10), 2077–2086. https://doi.org/10.1017/S0033291712003091

Fisher, Helen L., Appiah-Kusi, E., & Grant, C. (2012). Anxiety and negative self-schemas mediate the association between childhood maltreatment and paranoia. *Psychiatry Research*, *196*(2–3), 323–324. https://doi.org/10.1016/j.psychres.2011.12.004

Fisher, Helen L., Caspi, A., Moffitt, T. E., Wertz, J., Gray, R., Newbury, J., Ambler, A., Zavos, H., Danese, A., Mill, J., Odgers, C. L., Pariante, C., Wong, C. C. Y., & Arseneault, L. (2015). Measuring adolescents' exposure to victimization: The Environmental Risk (E-Risk) Longitudinal Twin Study. *Development and Psychopathology*, *27*(4pt2), 1399–1416. https://doi.org/10.1017/S0954579415000838

Fisher, Helen L., Jones, P. B., Fearon, P., Craig, T. K., Dazzan, P., Morgan, K., Hutchinson, G., Doody, G. A., McGuffin, P., Leff, J., Murray, R. M., & Morgan, C. (2010). The varying impact of type, timing and frequency of exposure to childhood adversity on its association with adult psychotic disorder. *Psychological Medicine*, *40*(12), 1967–1978. https://doi.org/10.1017/S0033291710000231

Fisher, Helen L., Schreier, A., Zammit, S., Maughan, B., Munafò, M. R., Lewis, G., & Wolke, D. (2013). Pathways Between Childhood Victimization and Psychosis-like Symptoms in the ALSPAC Birth Cohort. *Schizophrenia Bulletin*, *39*(5), 1045–1055. https://doi.org/10.1093/schbul/sbs088

FitzGerald, T. H. B., Hämmerer, D., Friston, K. J., Li, S.-C., & Dolan, R. J. (2017). Sequential inference as a mode of cognition and its correlates in fronto-parietal and hippocampal brain regions. *PLOS Computational Biology*, *13*(5), e1005418. https://doi.org/10.1371/journal.pcbi.1005418

Fletcher, P. C., & Frith, C. D. (2009). Perceiving is believing: A Bayesian approach to explaining the positive symptoms of schizophrenia. *Nature Reviews Neuroscience*, *10*(1), 48–58. https://doi.org/10.1038/nrn2536

Flouri, E. (2006). Parental interest in children's education, children's self-esteem and locus of control, and later educational attainment: Twenty-six year follow-up of the 1970 British Birth Cohort. *British Journal of Educational Psychology*, *76*(1), 41–55. https://doi.org/10.1348/000709905X52508

Fredstrom, B. K., Adams, R. E., & Gilman, R. (2011). Electronic and school-based victimization: Unique contexts for adjustment difficulties during adolescence. *Journal of Youth and Adolescence*, *40*(4), 405–415.

Freeman, D. (2007). Suspicious minds: The psychology of persecutory delusions. *Clinical Psychology Review*, *27*(4), 425–457. https://doi.org/10.1016/j.cpr.2006.10.004

Freeman, D., & Garety, P. (2014). Advances in understanding and treating persecutory delusions: A review. *Social Psychiatry and Psychiatric Epidemiology*, *49*(8), 1179–1189. https://doi.org/10.1007/s00127-014-0928-7

Freeman, D., Pugh, K., & Garety, P. (2008). Jumping to conclusions and paranoid ideation in the general population. *Schizophrenia Research*, *102*(1–3), 254–260. https://doi.org/10.1016/j.schres.2008.03.020

Frenkel, E., Kugelmass, S., Nathan, M., & Ingraham, L. J. (1995). Locus of control and mental health in adolescence and adulthood. *Schizophrenia Bulletin*, *21*(2), 219–226.

Frissen, A., Lieverse, R., Drukker, M., van Winkel, R., & Delespaul, P. (2015). Childhood trauma and childhood urbanicity in relation to psychotic disorder. *Social Psychiatry and Psychiatric Epidemiology*, *50*(10), 1481–1488. https://doi.org/10.1007/s00127-015-1049-7

Gage, S. H., Hickman, M., Heron, J., Munafò, M. R., Lewis, G., Macleod, J., & Zammit, S. (2014). Associations of cannabis and cigarette use with psychotic experiences at age 18: Findings from the Avon Longitudinal Study of Parents and Children. *Psychological Medicine*, *44*(16), 3435–3444. https://doi.org/10.1017/S0033291714000531

Gage, S. H., Jones, H. J., Burgess, S., Bowden, J., Davey Smith, G., Zammit, S., & Munafò, M. R. (2017). Assessing causality in associations between cannabis use and schizophrenia risk: A two-sample Mendelian randomization study. *Psychological Medicine*, *47*(5), 971–980. https://doi.org/10.1017/S0033291716003172

Garety, Kuipers, E., Fowler, D., Freeman, D., & Bebbington, P. E. (2001). A cognitive model of the positive symptoms of psychosis. *Psychological Medicine*, *31*(02), 189–195.

Garety, P. A. M. P., Hemsley, D. R. P. D., & Wessely, S. M. R. C. P. (1991). Reasoning in Deluded Schizophrenic and Paranoid Patients: Biases in Performance on a Probabilistic Inference Task. *Journal of Nervous*, *179*(4), 194–201.

Garety, P., Freeman, D., Jolley, S., Ross, K., Waller, H., & Dunn, G. (2011). Jumping to conclusions: The psychology of delusional reasoning. *Advances in Psychiatric Treatment*, *17*(5), 332–339. https://doi.org/10.1192/apt.bp.109.007104

Garety, P., Joyce, E., Jolley, S., Emsley, R., Waller, H., Kuipers, E., Bebbington, P., Fowler, D., Dunn, G., & Freeman, D. (2013). Neuropsychological functioning and jumping to conclusions in delusions. *Schizophrenia Research*, *150*(2–3), 570–574. https://doi.org/10.1016/j.schres.2013.08.035

Garety, P., Waller, H., Emsley, R., Jolley, S., Kuipers, E., Bebbington, P., Dunn, G., Fowler, D., Hardy, A., & Freeman, D. (2015). Cognitive Mechanisms of Change in Delusions: An Experimental Investigation Targeting Reasoning to Effect Change in Paranoia. *Schizophrenia Bulletin*, *41*(2), 400–410. https://doi.org/10.1093/schbul/sbu103

Gawęda, Ł., Krężołek, M., Olbryś, J., Turska, A., & Kokoszka, A. (2015). Decreasing self-reported cognitive biases and increasing clinical insight through meta-cognitive training in patients with chronic schizophrenia. *Journal of Behavior Therapy and Experimental Psychiatry*, *48*, 98–104. https://doi.org/10.1016/j.jbtep.2015.02.002

Gawęda, Ł., Pionke, R., Krężołek, M., Prochwicz, K., Kłosowska, J., Frydecka, D., Misiak, B., Kotowicz, K., Samochowiec, A., Mak, M., Błądziński, P., Cechnicki, A., & Nelson, B. (2018). Self-disturbances, cognitive biases and insecure attachment as mechanisms of the relationship between traumatic life events and psychotic-like experiences in non-clinical adults—A path analysis. *Psychiatry Research*, *259*, 571–578. https://doi.org/10.1016/j.psychres.2017.11.009

Gawęda, Ł., Prochwicz, K., Adamczyk, P., Frydecka, D., Misiak, B., Kotowicz, K., Szczepanowski, R., Florkowski, M., & Nelson, B. (2018). The role of self-disturbances and cognitive biases in the relationship between traumatic life events and psychosis proneness in a non-clinical sample. *Schizophrenia Research*, *193*, 218–224. https://doi.org/10.1016/j.schres.2017.07.023

Gejman, P., Sanders, A., & Duan, J. (2010). The Role of Genetics in the Etiology of Schizophrenia. *The Psychiatric Clinics of North America*, *33*(1), 35–66. https://doi.org/10.1016/j.psc.2009.12.003

Gelder, M. G. (1996). *Oxford textbook of psychiatry*. Oxford University Press,.

Gibson, L. E., Alloy, L. B., & Ellman, L. M. (2016). Trauma and the psychosis spectrum: A review of symptom specificity and explanatory mechanisms. *Clinical Psychology Review*, *49*, 92–105. https://doi.org/10.1016/j.cpr.2016.08.003

Global Burden of Disease Study 2013 Collaborators. (2015). Global, regional, and national incidence, prevalence, and years lived with disability for 301 acute and chronic diseases and injuries in 188 countries, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. *Lancet (London, England)*, *386*(9995), 743–800. https://doi.org/10.1016/S0140-6736(15)60692-4

Goldberg, L. R., & Freyd, J. J. (2006). Self-reports of potentially traumatic experiences in an adult community sample: Gender differences and test-retest stabilities of the items in a brief betrayal-trauma survey. *Journal of Trauma & Dissociation: The Official Journal of the International Society for the Study of Dissociation (ISSD)*, *7*(3), 39–63. https://doi.org/10.1300/J229v07n03_04

Golding, J., Pembrey, M., Jones, R., & ALSPAC Study Team. (2001). ALSPAC--the Avon Longitudinal Study of Parents and Children. I. Study methodology. *Paediatric and Perinatal Epidemiology*, *15*(1), 74–87.

Gonçalves, F. G., Heldt, E., Peixoto, B. N., Rodrigues, G. A., Filipetto, M., & Guimarães, L. S. P. (2016). Construct validity and reliability of Olweus Bully/Victim Questionnaire – Brazilian version. *Psicologia: Reflexão e Crítica*, *29*(1), 27. https://doi.org/10.1186/s41155-016-0019-7

González, L. E., López-Carrilero, R., Barrigón, M. L., Grasa, E., Barajas, A., Pousa, E., González-Higueras, F., Ruiz-Delgado, I., Cid, J., Lorente-Rovira, E., Pélaez, T., & Ochoa, S. (2018). Neuropsychological functioning and jumping to conclusions in recent onset psychosis patients. *Schizophrenia Research*, *195*, 366–371. https://doi.org/10.1016/j.schres.2017.09.039

Goodwin, R. D., & Stein, M. B. (2004). Association between childhood trauma and physical disorders among adults in the United States. *Psychological Medicine*, *34*(3), 509–520. https://doi.org/10.1017/S003329170300134X

Griffin, J. D., & Fletcher, P. C. (2017). Predictive Processing, Source Monitoring, and Psychosis. *Annual Review of Clinical Psychology*, *13*, 265–289. https://doi.org/10.1146/annurev-clinpsy-032816-045145

Gunnar, M. R., Wewerka, S., Frenn, K., Long, J. D., & Griggs, C. (2009). Developmental changes in hypothalamus-pituitary-adrenal activity over the transition to adolescence: Normative changes and associations with puberty. *Development and Psychopathology*, *21*(1), 69–85. https://doi.org/10.1017/S0954579409000054

Gur, R. E., Moore, T. M., Rosen, A. F. G., Barzilay, R., Roalf, D. R., Calkins, M. E., Ruparel, K., Scott, J. C., Almasy, L., Satterthwaite, T. D., Shinohara, R. T., & Gur, R. C. (2019). Burden of Environmental Adversity Associated With Psychopathology, Maturation, and Brain Behavior Parameters in Youths. *JAMA Psychiatry*. https://doi.org/10.1001/jamapsychiatry.2019.0943

Hameed, M. A., Lingam, R., Zammit, S., Salvi, G., Sullivan, S., & Lewis, A. J. (2018). Trajectories of Early Childhood Developmental Skills and Early Adolescent Psychotic Experiences: Findings from the ALSPAC UK Birth Cohort. *Frontiers in Psychology*, *8*. https://doi.org/10.3389/fpsyg.2017.02314

Hardy, A. (2017). Pathways from Trauma to Psychotic Experiences: A Theoretically Informed Model of Posttraumatic Stress in Psychosis. *Frontiers in Psychology*, *8*. https://doi.org/10.3389/fpsyg.2017.00697

Hardy, A., Emsley, R., Freeman, D., Bebbington, P., Garety, P. A., Kuipers, E. E., Dunn, G., & Fowler, D. (2016). Psychological Mechanisms Mediating Effects Between Trauma and Psychotic Symptoms: The Role of Affect Regulation, Intrusive Trauma Memory, Beliefs, and Depression. *Schizophrenia Bulletin*, *42*(suppl_1), S34–S43. https://doi.org/10.1093/schbul/sbv175

Harrow, M., Hansford, B. G., & Astrachan-Fletcher, E. B. (2009). Locus of control: Relation to schizophrenia, to recovery, and to depression and psychosis — A 15-year longitudinal study. *Psychiatry Research*, *168*(3), 186–192. https://doi.org/10.1016/j.psychres.2008.06.002

Healy, C., Brannigan, R., Dooley, N., Coughlan, H., Clarke, M., Kelleher, I., & Cannon, M. (2019a). Childhood and adolescent psychotic experiences and risk of mental disorder: A systematic review and meta-analysis. *Psychological Medicine*, 1–11. https://doi.org/10.1017/S0033291719000485

Healy, C., Brannigan, R., Dooley, N., Coughlan, H., Clarke, M., Kelleher, I., & Cannon, M. (2019b). Childhood and adolescent psychotic experiences and risk of mental disorder: A systematic review and meta-analysis. *Psychological Medicine*, *49*(10), 1589–1599. https://doi.org/10.1017/S0033291719000485

Heins, M., Simons, C., Lataster, T., Pfeifer, S., Versmissen, D., Lardinois, M., Marcelis, M., Delespaul, P., Krabbendam, L., van Os, J., & Myin-Germeys, I. (2011). Childhood trauma and psychosis: A case-control and case-sibling comparison across different levels of genetic liability, psychopathology, and type of trauma. *The American Journal of Psychiatry*, *168*(12), 1286–1294. https://doi.org/10.1176/appi.ajp.2011.10101531

Heinz, A., Deserno, L., & Reininghaus, U. (2013). Urbanicity, social adversity and psychosis. *World Psychiatry*, *12*(3), 187–197. https://doi.org/10.1002/wps.20056

Herbison, C. E., Allen, K., Robinson, M., Newnham, J., & Pennell, C. (2017). The impact of life stress on adult depression and anxiety is dependent on gender and timing of exposure. *Development and Psychopathology*, *29*(4), 1443–1454. https://doi.org/10.1017/S0954579417000372

Hermann von Helmholtz. (1924). *Helmholtz's treatise on physiological optics / translated from the 3rd German ed. ; Edited by James P.C. Southall.* Optical Society of America.

Higgins, J. P. T., Green, S., & Cochrane Collaboration. (2008). *Cochrane handbook for systematic reviews of interventions*. Wiley-Blackwell. https://www.dawsonera.com/guard/protected/dawson.jsp?name=https://idp.bris.ac.uk/shibboleth&dest=http://www.dawsonera.com/depp/reader/protected/external/AbstractView/S9780470712177

Higgins, J. P. T., & Thompson, S. G. (2002). Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine*, *21*(11), 1539–1558. https://doi.org/10.1002/sim.1186

Hilker, R., Helenius, D., Fagerlund, B., Skytthe, A., Christensen, K., Werge, T. M., Nordentoft, M., & Glenthøj, B. (2018). Heritability of Schizophrenia and Schizophrenia Spectrum Based on the Nationwide Danish Twin Register. *Biological Psychiatry*, *83*(6), 492–498. https://doi.org/10.1016/j.biopsych.2017.08.017

Hill, A. B. (1965). The Environment and Disease: Association or Causation? *Proceedings of the Royal Society of Medicine*, *58*(5), 295–300.

Hjorthøj, C., Stürup, A. E., McGrath, J. J., & Nordentoft, M. (2017). Years of potential life lost and life expectancy in schizophrenia: A systematic review and meta-analysis. *The Lancet Psychiatry*. https://doi.org/10.1016/S2215-0366(17)30078-0

Holder, E. E., & Levi, D. J. (1988). Mental health and locus of control: SCL-90-R and Levenson's IPC scales. *Journal of Clinical Psychology*, *44*(5), 753–755. https://doi.org/10.1002/1097-4679(198809)44:5<753::AID-JCLP2270440514>3.0.CO;2-A

Hollander, A.-C., Dal, H., Lewis, G., Magnusson, C., Kirkbride, J. B., & Dalman, C. (2016). Refugee migration and risk of schizophrenia and other non-affective psychoses: Cohort study of 1.3 million people in Sweden. *BMJ*, *352*, i1030. https://doi.org/10.1136/bmj.i1030

Horwood, J., Thomas, K., Duffy, L., Gunnell, D., Hollis, C., Lewis, G., Thompson, A., Wolke, D., Zammitt, S., & Harrison, G. (2008). Frequency of psychosis-like symptoms in a non-clinical population of 12 year olds: Results from the Alspac birth cohort. *European Psychiatry*, *23*, *Supplement 2*, S282. https://doi.org/10.1016/j.eurpsy.2008.01.595

Horwood, Jeremy, Salvi, G., Thomas, K., Duffy, L., Gunnell, D., Hollis, C., Lewis, G., Menezes, P., Thompson, A., Wolke, D., Zammit, S., & Harrison, G. (2008). IQ and non-clinical psychotic symptoms in 12-year-olds: Results from the ALSPAC birth cohort. *The British Journal of Psychiatry*, *193*(3), 185–191. https://doi.org/10.1192/bjp.bp.108.051904

Houtepen, L. C., Heron, J., Suderman, M. J., Tilling, K., & Howe, L. D. (2018). Adverse childhood experiences in the children of the Avon Longitudinal Study of Parents and Children (ALSPAC). *Wellcome Open Research*, *3*. https://doi.org/10.12688/wellcomeopenres.14716.1

Hovens, J. G. F. M., Giltay, E. J., Wiersma, J. E., Spinhoven, P., Penninx, B. W. J. H., & Zitman, F. G. (2012). Impact of childhood life events and trauma on the course of depressive and anxiety disorders. *Acta Psychiatrica Scandinavica*, *126*(3), 198–207. https://doi.org/10.1111/j.1600-0447.2011.01828.x

Hovens, Jacqueline G. F. M., Giltay, E. J., van Hemert, A. M., & Penninx, B. W. J. H. (2016). CHILDHOOD MALTREATMENT AND THE COURSE OF DEPRESSIVE AND ANXIETY DISORDERS: THE CONTRIBUTION OF PERSONALITY CHARACTERISTICS. *Depression and Anxiety*, *33*(1), 27–34.

Howe, J., Ross, R., McKay, R., & Balzan, R. P. (2018). How Do Delusion-Prone Individuals Respond to Disconfirmatory Evidence?: Improving Comprehension of the Beads Task May Help. *Zeitschrift Für Psychologie*, *226*(3), 182–190. https://doi.org/10.1027/2151-2604/a000333

Howe, L. D., Tilling, K., Galobardes, B., & Lawlor, D. A. (2013). Loss to follow-up in cohort studies: Bias in estimates of socioeconomic inequalities. *Epidemiology (Cambridge, Mass.)*, *24*(1), 1–9. https://doi.org/10.1097/EDE.0b013e31827623b1

Howes, O. D., & Kapur, S. (2009). The Dopamine Hypothesis of Schizophrenia: Version III--The Final Common Pathway. *Schizophrenia Bulletin*, *35*(3), 549–562. https://doi.org/10.1093/schbul/sbp006

Howes, Oliver D, McCutcheon, R., Owen, M. J., & Murray, R. (2017). The role of genes, stress and dopamine in the development of schizophrenia. *Biological Psychiatry*, *81*(1), 9–20. https://doi.org/10.1016/j.biopsych.2016.07.014

Huang, H., Yan, P., Shan, Z., Chen, S., Li, M., Luo, C., Gao, H., Hao, L., & Liu, L. (2015). Adverse childhood experiences and risk of type 2 diabetes: A systematic review and meta-analysis. *Metabolism*, *64*(11), 1408–1418. https://doi.org/10.1016/j.metabol.2015.08.019

Hubbard, L., Tansey, K. E., Rai, D., Jones, P., Ripke, S., Chambert, K. D., Moran, J. L., McCarroll, S. A., Linden, D. E. J., Owen, M. J., O'Donovan, M. C., Walters, J. T. R., & Zammit, S. (2016). Evidence of

Common Genetic Overlap Between Schizophrenia and Cognition. *Schizophrenia Bulletin*, *42*(3), 832–842. https://doi.org/10.1093/schbul/sbv168

Hutton, P., Morrison, A. P., Wardle, M., & Wells, A. (2014). Metacognitive Therapy in Treatment-Resistant Psychosis: A Multiple-Baseline Study. *Behavioural and Cognitive Psychotherapy*, *42*(2), 166–185. https://doi.org/10.1017/S1352465812001026

Iles-Caven, Y., Golding, J., Gregory, S., Emond, A., & Taylor, C. M. (2016). Data relating to early child development in the Avon Longitudinal Study of Parents and Children (ALSPAC), their relationship with prenatal blood mercury and stratification by fish consumption. *Data in Brief*, *9*, 112–122. https://doi.org/10.1016/j.dib.2016.08.034

Isvoranu, A.-M., Borkulo, C. D. van, Boyette, L.-L., Wigman, J. T. W., Vinkers, C. H., Borsboom, D., & Investigators, G. (2016). A Network Approach to Psychosis: Pathways Between Childhood Trauma and Psychotic Symptoms. *Schizophrenia Bulletin*, sbw055. https://doi.org/10.1093/schbul/sbw055

It's time to talk about ditching statistical significance. (2019). *Nature*. https://www.nature.com/articles/d41586-019-00874-8

Jablensky, A. (2000). Epidemiology of schizophrenia: The global burden of disease and disability. *European Archives of Psychiatry and Clinical Neuroscience*, *250*(6), 274–285. https://doi.org/10.1007/s004060070002

Jablensky, A., McNeil, T. F., & Morgan, V. A. (2017). Barbara Fish and a Short History of the Neurodevelopmental Hypothesis of Schizophrenia. *Schizophrenia Bulletin*, *43*(6), 1158–1163. https://doi.org/10.1093/schbul/sbx094

Janssen, I., Krabbendam, L., Bak, M., Hanssen, M., Vollebergh, W., de Graaf, R., & van Os, J. (2004). Childhood abuse as a risk factor for psychotic experiences. *Acta Psychiatrica Scandinavica*, *109*(1), 38–45. https://doi.org/10.1046/j.0001-690X.2003.00217.x

Janssen, I., Versmissen, D., Campo, J. À., Myin-Germeys, I., Os, J. V., & Krabbendam, L. (2006). Attribution style and psychosis: Evidence for an externalizing bias in patients but not in individuals at high risk. *Psychological Medicine*, *36*(6), 771–778. https://doi.org/10.1017/S0033291706007422

Jardri, R., Duverne, S., Litvinova, A. S., & Denève, S. (2017). Experimental evidence for circular inference in schizophrenia. *Nature Communications*, *8*, 14218. https://doi.org/10.1038/ncomms14218

Jardri, R., Hugdahl, K., Hughes, M., Brunelin, J., Waters, F., Alderson-Day, B., Smailes, D., Sterzer, P., Corlett, P. R., Leptourgos, P., Debbané, M., Cachia, A., & Denève, S. (2016). Are Hallucinations Due to an

Imbalance Between Excitatory and Inhibitory Influences on the Brain? *Schizophrenia Bulletin*, *42*(5), 1124–1134. https://doi.org/10.1093/schbul/sbw075

Jauhar, S., Nour, M. M., Veronese, M., Rogdaki, M., Bonoldi, I., Azis, M., Turkheimer, F., McGuire, P., Young, A. H., & Howes, O. D. (2017). A Test of the Transdiagnostic Dopamine Hypothesis of Psychosis Using Positron Emission Tomographic Imaging in Bipolar Affective Disorder and Schizophrenia. *JAMA Psychiatry*, *74*(12), 1206–1213. https://doi.org/10.1001/jamapsychiatry.2017.2943

Jiménez-Barbero, J. A., Ruiz-Hernández, J. A., Llor-Zaragoza, L., Pérez-García, M., & Llor-Esteban, B. (2016). Effectiveness of anti-bullying school programs: A meta-analysis. *Children and Youth Services Review*, *61*, 165–175. https://doi.org/10.1016/j.childyouth.2015.12.015

Jolley, S., Garety, P., Bebbington, P., Dunn, G., Freeman, D., Kuipers, E., Fowler, D., & Hemsley, D. (2006). Attributional style in psychosis—The role of affect and belief type. *Behaviour Research and Therapy*, *44*(11), 1597–1607. https://doi.org/10.1016/j.brat.2005.12.002

Jolley, S., Thompson, C., Hurley, J., Medin, E., Butler, L., Bebbington, P., Dunn, G., Freeman, D., Fowler, D., Kuipers, E., & Garety, P. (2014). Jumping to the wrong conclusions? An investigation of the mechanisms of reasoning errors in delusions. *Psychiatry Research*, *219*(2), 275–282. https://doi.org/10.1016/j.psychres.2014.05.051

Jones, H. J., Gage, S. H., Heron, J., Hickman, M., Lewis, G., Munafò, M. R., & Zammit, S. (2018). Association of Combined Patterns of Tobacco and Cannabis Use in Adolescence With Psychotic Experiences. *JAMA Psychiatry*, *75*(3), 240–246. https://doi.org/10.1001/jamapsychiatry.2017.4271

Jones, H. J., Stergiakouli, E., Tansey, K. E., Hubbard, L., Heron, J., Cannon, M., Holmans, P., Lewis, G., Linden, D. E. J., Jones, P. B., Smith, G. D., O'Donovan, M. C., Owen, M. J., Walters, J. T., & Zammit, S. (2016). Phenotypic Manifestation of Genetic Risk for Schizophrenia During Adolescence in the General Population. *JAMA Psychiatry*, *73*(3), 221–228. https://doi.org/10.1001/jamapsychiatry.2015.3058

Kaney, S., & Bentall, R. P. (1989). Persecutory delusions and attributional style. *British Journal of Medical Psychology*, *62*(2), 191–198. https://doi.org/10.1111/j.2044-8341.1989.tb02826.x

Kapur, S. (2003). Psychosis as a State of Aberrant Salience: A Framework Linking Biology, Phenomenology, and Pharmacology in Schizophrenia. *American Journal of Psychiatry*, *160*(1), 13–23. https://doi.org/10.1176/appi.ajp.160.1.13

Kapur, S., & Mamo, D. (2003). Half a century of antipsychotics and still a central role for dopamine D2 receptors. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *27*(7), 1081–1090. https://doi.org/10.1016/j.pnpbp.2003.09.004

Katthagen, T., Dammering, F., Kathmann, N., Kaminski, J., Walter, H., Heinz, A., & Schlagenhauf, F. (2016). Validating the construct of aberrant salience in schizophrenia—Behavioral evidence for an automatic process. *Schizophrenia Research: Cognition*, *6*, 22–27. https://doi.org/10.1016/j.scog.2016.10.001

Katthagen, T., Mathys, C., Deserno, L., Walter, H., Kathmann, N., Heinz, A., & Schlagenhauf, F. (2018). Modeling subjective relevance in schizophrenia and its relation to aberrant salience. *PLOS Computational Biology*, *14*(8), e1006319. https://doi.org/10.1371/journal.pcbi.1006319

Kaymaz, N., Drukker, M., Lieb, R., Wittchen, H.-U., Werbeloff, N., Weiser, M., Lataster, T., & Os, J. van. (2012). Do subthreshold psychotic experiences predict clinical outcomes in unselected non-help-seeking population-based samples? A systematic review and meta-analysis, enriched with new results. *Psychological Medicine*, *42*(11), 2239–2253. https://doi.org/10.1017/S0033291711002911

Kaymaz, N., & van Os, J. (2010). Extended psychosis phenotype--yes: Single continuum--unlikely. *Psychological Medicine*, *40*(12), 1963–1966. https://doi.org/10.1017/S0033291710000358

Kaymaz, Nil, Krabbendam, L., de Graaf, R., Nolen, W., ten Have, M., & van Os, J. (2006). Evidence that the urban environment specifically impacts on the psychotic but not the affective dimension of bipolar disorder. *Social Psychiatry and Psychiatric Epidemiology*, *41*(9), 679–685. https://doi.org/10.1007/s00127-006-0086-7

Kelleher, I., Connor, D., Clarke, M. C., Devlin, N., Harley, M., & Cannon, M. (2012). Prevalence of psychotic symptoms in childhood and adolescence: A systematic review and meta-analysis of population-based studies. *Psychological Medicine*, *42*(9), 1857–1863. https://doi.org/10.1017/S0033291711002960

Kelleher, Ian, Keeley, H., Corcoran, P., Ramsay, H., Wasserman, C., Carli, V., Sarchiapone, M., Hoven, C., Wasserman, D., & Cannon, M. (2013). Childhood trauma and psychosis in a prospective cohort study: Cause, effect, and directionality. *The American Journal of Psychiatry*, *170*(7), 734–741. https://doi.org/10.1176/appi.ajp.2012.12091169

Khandaker, G. M., Stochl, J., Zammit, S., Lewis, G., & Jones, P. B. (2014). A population-based longitudinal study of childhood neurodevelopmental disorders, IQ and subsequent risk of psychotic experiences in adolescence. *Psychological Medicine*, *44*(15), 3229–3238. https://doi.org/10.1017/S0033291714000750

Khandaker, G. M., Zimbron, J., Lewis, G., & Jones, P. B. (2013). Prenatal maternal infection, neurodevelopment and adult schizophrenia: A systematic review of population-based studies. *Psychological Medicine*, *43*(2), 239–257. https://doi.org/10.1017/S0033291712000736

Khandaker, Golam M., Barnett, J. H., White, I. R., & Jones, P. B. (2011). A quantitative meta-analysis of population-based studies of premorbid intelligence and schizophrenia. *Schizophrenia Research*, *132*(2–3), 220–227. https://doi.org/10.1016/j.schres.2011.06.017

Khandaker, Golam M., Stochl, J., Zammit, S., Lewis, G., & Jones, P. B. (2014). Childhood Epstein-Barr Virus infection and subsequent risk of psychotic experiences in adolescence: A population-based prospective serological study. *Schizophrenia Research*, *158*(1), 19–24. https://doi.org/10.1016/j.schres.2014.05.019

Kirkbride, J. B., Boydell, J., Ploubidis, G. B., Morgan, C., Dazzan, P., McKenzie, K., Murray, R. M., & Jones, P. B. (2008). Testing the association between the incidence of schizophrenia and social capital in an urban area. *Psychological Medicine*, *38*(8), 1083–1094. https://doi.org/10.1017/S0033291707002085

Kirkbride, J. B., Jones, P. B., Ullrich, S., & Coid, J. W. (2014). Social Deprivation, Inequality, and the Neighborhood-Level Incidence of Psychotic Syndromes in East London. *Schizophrenia Bulletin*, *40*(1), 169–180. https://doi.org/10.1093/schbul/sbs151

Kirkbride, James B., Errazuriz, A., Croudace, T. J., Morgan, C., Jackson, D., Boydell, J., Murray, R. M., & Jones, P. B. (2012). Incidence of Schizophrenia and Other Psychoses in England, 1950–2009: A Systematic Review and Meta-Analyses. *PLOS ONE*, *7*(3), e31660. https://doi.org/10.1371/journal.pone.0031660

Kirkbride, James B., Fearon, P., Morgan, C., Dazzan, P., Morgan, K., Tarrant, J., Lloyd, T., Holloway, J., Hutchinson, G., Leff, J. P., Mallett, R. M., Harrison, G. L., Murray, R. M., & Jones, P. B. (2006). Heterogeneity in incidence rates of schizophrenia and other psychotic syndromes: Findings from the 3-center AeSOP study. *Archives of General Psychiatry*, *63*(3), 250–258. https://doi.org/10.1001/archpsyc.63.3.250

Kirkwood, & Sterne. (2003). *Essential Medical Statistics* (2nd ed.). Wiley.

Kisely, S., Abajobir, A. A., Mills, R., Strathearn, L., Clavarino, A., & Najman, J. M. (2018). Child maltreatment and mental health problems in adulthood: Birth cohort study. *The British Journal of Psychiatry*, *213*(6), 698–703. https://doi.org/10.1192/bjp.2018.207

Kırlı, U., Binbay, T., Drukker, M., Elbi, H., Kayahan, B., Keskin Gökçelli, D., Özkınay, F., Onay, H., Alptekin, K., & van Os, J. (2019). DSM outcomes of psychotic experiences and associated risk factors: 6-year follow-up study in a community-based sample. *Psychological Medicine*, *49*(8), 1346–1356. https://doi.org/10.1017/S0033291718001964

Klein, H. S., & Pinkham, A. E. (2018). Examining reasoning biases in schizophrenia using a modified ‘Jumping to Conclusions’ probabilistic reasoning task. *Psychiatry Research*, *270*, 180–186. https://doi.org/10.1016/j.psychres.2018.09.020

Knack, J. M., Jensen-Campbell, L. A., & Baum, A. (2011). Worse than sticks and stones? Bullying is associated with altered HPA axis functioning and poorer health. *Brain and Cognition*, *77*(2), 183–190. https://doi.org/10.1016/j.bandc.2011.06.011

Kohler, C. G., Walker, J. B., Martin, E. A., Healey, K. M., & Moberg, P. J. (2010). Facial Emotion Perception in Schizophrenia: A Meta-analytic Review. *Schizophrenia Bulletin*, *36*(5), 1009–1019. https://doi.org/10.1093/schbul/sbn192

Kraan, T., Velthorst, E., Smit, F., de Haan, L., & van der Gaag, M. (2015). Trauma and recent life events in individuals at ultra high risk for psychosis: Review and meta-analysis. *Schizophrenia Research*, *161*(2–3), 143–149. https://doi.org/10.1016/j.schres.2014.11.026

Kube, T., Schwarting, R., Rozenkrantz, L., Glombiewski, J. A., & Rief, W. (2019). Distorted Cognitive Processes in Major Depression: A Predictive Processing Perspective. *Biological Psychiatry*. https://doi.org/10.1016/j.biopsych.2019.07.017

Kuipers, E., Garety, P., Fowler, D., Freeman, D., Dunn, G., & Bebbington, P. (2006). Cognitive, Emotional, and Social Processes in Psychosis: Refining Cognitive Behavioral Therapy for Persistent Positive Symptoms. *Schizophrenia Bulletin*, *32*(Suppl 1), S24–S31. https://doi.org/10.1093/schbul/sbl014

Langdon, R., Ward, P. B., & Coltheart, M. (2010). Reasoning Anomalies Associated With Delusions in Schizophrenia. *Schizophrenia Bulletin*, *36*(2), 321–330. https://doi.org/10.1093/schbul/sbn069

Langdon, Robyn, Still, M., Connors, M. H., Ward, P. B., & Catts, S. V. (2013). Attributional biases, paranoia, and depression in early psychosis. *British Journal of Clinical Psychology*, *52*(4), 408–423. https://doi.org/10.1111/bjc.12026

Langdon, Robyn, Still, M., Connors, M. H., Ward, P. B., & Catts, S. V. (2014). Jumping to delusions in early psychosis. *Cognitive Neuropsychiatry*, *19*(3), 241–256. https://doi.org/10.1080/13546805.2013.854198

Lardinois, M., Lataster, T., Mengelers, R., Van Os, J., & Myin-Germeys, I. (2011). Childhood trauma and increased stress sensitivity in psychosis. *Acta Psychiatrica Scandinavica*, *123*(1), 28–35. https://doi.org/10.1111/j.1600-0447.2010.01594.x

Larsson, S., Andreassen, O. A., Aas, M., Røssberg, J. I., Mork, E., Steen, N. E., Barrett, E. A., Lagerberg, T. V., Peleikis, D., Agartz, I., Melle, I., & Lorentzen, S. (2013). High prevalence of childhood trauma in patients with schizophrenia spectrum and affective disorder. *Comprehensive Psychiatry*, *54*(2), 123–127. https://doi.org/10.1016/j.comppsych.2012.06.009

Lataster, J., Myin-Germeys, I., Lieb, R., Wittchen, H.-U., & Os, J. van. (2012). Adversity and psychosis: A 10-year prospective study investigating synergism between early and recent adversity in psychosis. *Acta Psychiatrica Scandinavica*, *125*(5), 388–399. https://doi.org/10.1111/j.1600-0447.2011.01805.x

Lataster, T., Os, J. van, Drukker, M., Henquet, C., Feron, F., Gunther, N., & Myin-Germeys, I. (2006). Childhood victimisation and developmental expression of non-clinical delusional ideation and hallucinatory experiences. *Social Psychiatry and Psychiatric Epidemiology*, *41*(6), 423–428. https://doi.org/10.1007/s00127-006-0060-4

Lauber, C., Keller, C., Eichenberger, A., & Rössler, W. (2005). Family burden during exacerbation of schizophrenia: Quantification and determinants of additional costs. *The International Journal of Social Psychiatry*, *51*(3), 259–264. https://doi.org/10.1177/0020764005057376

Lawrie, S. M. (2016). Whether "psychosis" is best conceptualized as a continuum or in categories is an empirical, practical and political question. *World Psychiatry*, *15*(2), 125–126. https://doi.org/10.1002/wps.20325

Lecei, A., Decoster, J., De Hert, M., Derom, C., Jacobs, N., Menne-Lothmann, C., van Os, J., Thiery, E., Rutten, B. P. F., Wichers, M., & van Winkel, R. (2019). Evidence that the association of childhood trauma with psychosis and related psychopathology is not explained by gene-environment correlation: A monozygotic twin differences approach. *Schizophrenia Research*, *205*, 58–62. https://doi.org/10.1016/j.schres.2018.05.025

Lee, K.-W., Chan, K.-W., Chang, W.-C., Lee, E. H.-M., Hui, C. L.-M., & Chen, E. Y.-H. (2016). A systematic review on definitions and assessments of psychotic-like experiences. *Early Intervention in Psychiatry*, *10*(1), 3–16. https://doi.org/10.1111/eip.12228

Legge, S. E., Jones, H. J., Kendall, K. M., Pardiñas, A. F., Menzies, G., Bracher-Smith, M., Escott-Price, V., Rees, E., Davis, K. A. S., Hotopf, M., Savage, J. E., Posthuma, D., Holmans, P., Kirov, G., Owen, M. J., O'Donovan, M. C., Zammit, S., & Walters, J. T. R. (2019). Association of Genetic Liability to Psychotic Experiences With Neuropsychotic Disorders and Traits. *JAMA Psychiatry*. https://doi.org/10.1001/jamapsychiatry.2019.2508

Lenz, A. S., & Hollenbaugh, K. M. (2015). Meta-Analysis of Trauma-Focused Cognitive Behavioral Therapy for Treating PTSD and Co-occurring Depression Among Children and Adolescents. *Counseling Outcome Research and Evaluation*, *6*(1), 18–32. https://doi.org/10.1177/2150137815573790

Leppert, B., Havdahl, A., Riglin, L., Jones, H. J., Zheng, J., Smith, G. D., Tilling, K., Thapar, A., Reichborn-Kjennerud, T., & Stergiakouli, E. (2019). Association of Maternal Neurodevelopmental Risk Alleles With Early-Life Exposures. *JAMA Psychiatry*. https://doi.org/10.1001/jamapsychiatry.2019.0774

Levin, M. L. (1953). The occurrence of lung cancer in man. *Acta - Unio Internationalis Contra Cancrum*, *9*(3), 531–541.

Lewis, S. J., Arseneault, L., Caspi, A., Fisher, H. L., Matthews, T., Moffitt, T. E., Odgers, C. L., Stahl, D., Teng, J. Y., & Danese, A. (2019). The epidemiology of trauma and post-traumatic stress disorder in a representative cohort of young people in England and Wales. *The Lancet Psychiatry*, *6*(3), 247–256. https://doi.org/10.1016/S2215-0366(19)30031-8

Li, R., Ma, X., Wang, G., Yang, J., & Wang, C. (2016). Why sex differences in schizophrenia? *Journal of Translational Neuroscience*, *1*(1), 37–42.

Lincoln, T. M., Marin, N., & Jaya, E. S. (n.d.). Childhood trauma and psychotic experiences in a general population sample: A prospective study on the mediating role of emotion regulation. *European Psychiatry*. https://doi.org/10.1016/j.eurpsy.2016.12.010

Lincoln, Tania M., Lange, J., Burau, J., Exner, C., & Moritz, S. (2010). The Effect of State Anxiety on Paranoid Ideation and Jumping to Conclusions. An Experimental Investigation. *Schizophrenia Bulletin*, *36*(6), 1140–1148. https://doi.org/10.1093/schbul/sbp029

Linscott, R. J., & Os, J. van. (2013). An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: On the pathway from proneness to persistence to dimensional expression across mental disorders. *Psychological Medicine*, *43*(6), 1133–1149. https://doi.org/10.1017/S0033291712001626

Longden, E., Sampson, M., & Read, J. (2016). Childhood adversity and psychosis: Generalised or specific effects? *Epidemiology and Psychiatric Sciences*, *25*(4), 349–359. https://doi.org/10.1017/S204579601500044X

Luciano, S., & Savage, R. S. (2007). Bullying risk in children with learning difficulties in inclusive educational settings. *Canadian Journal of School Psychology*, *22*(1), 14–31.

Lupien, S. J., McEwen, B. S., Gunnar, M. R., & Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nature Reviews Neuroscience*, *10*(6), 434–445. https://doi.org/10.1038/nrn2639

Lurie, S., Boaz, M., & Golan, A. (2013). Risk factors for rape re-victimisation: A retrospective analysis. *Journal of Obstetrics and Gynaecology*, *33*(8), 865–867. https://doi.org/10.3109/01443615.2013.829031

Mackie, C. J., O'Leary-Barrett, M., Al-Khudhairy, N., Castellanos-Ryan, N., Struve, M., Topper, L., & Conrod, P. (2013). Adolescent bullying, cannabis use and emerging psychotic experiences: A longitudinal general population study. *Psychological Medicine*, *43*(5), 1033–1044. https://doi.org/10.1017/S003329171200205X

Maijer, K., Begemann, M. J. H., Palmen, S. J. M. C., Leucht, S., & Sommer, I. E. C. (2018). Auditory hallucinations across the lifespan: A systematic review and meta-analysis. *Psychological Medicine*, *48*(6), 879–888. https://doi.org/10.1017/S0033291717002367

Mäkikyrö, T., Sauvola, A., Moring, J., Veijola, J., Nieminen, P., Järvelin, M. R., & Isohanni, M. (1998). Hospital-treated psychiatric disorders in adults with a single-parent and two-parent family background: A 28-year follow-up of the 1966 Northern Finland Birth Cohort. *Family Process*, *37*(3), 335–344.

Mancuso, F., Horan, W. P., Kern, R. S., & Green, M. F. (2011). Social cognition in psychosis: Multidimensional structure, clinical correlates, and relationship with functional outcome. *Schizophrenia Research*, *125*(2–3), 143–151. https://doi.org/10.1016/j.schres.2010.11.007

Mandavia, A., Robinson, G. G. N., Bradley, B., Ressler, K. J., & Powers, A. (2016). Exposure to Childhood Abuse and Later Substance Use: Indirect Effects of Emotion Dysregulation and Exposure to Trauma. *Journal of Traumatic Stress*, *29*(5), 422–429. https://doi.org/10.1002/jts.22131

Manly, T., Anderson, V., Nimmo-Smith, I., Turner, A., Watson, P., & Robertson, I. H. (2001). The differential assessment of children's attention: The Test of Everyday Attention for Children (TEA-Ch), normative sample and ADHD performance. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *42*(8), 1065–1081.

Mannarino, A. P., & Cohen, J. A. (1996). Abuse-Related Attributions and Perceptions, General Attributions, and Locus of Control in Sexually Abused Girls ,
Abuse-Related Attributions and Perceptions, General Attributions, and Locus of Control in Sexually Abused Girls. *Journal of Interpersonal Violence*, *11*(2), 162–180. https://doi.org/10.1177/088626096011002002

Mannarino, A. P., Cohen, J. A., & Berman, S. R. (1994). The children's attributions and perceptions scale: A new measure of sexual abuse-related factors. *Journal of Clinical Child Psychology*, *23*(2), 204–211. https://doi.org/10.1207/s15374424jccp2302_9

Mansueto, G., Schruers, K., Cosci, F., van Os, J., Alizadeh, B. Z., Bartels-Velthuis, A. A., van Beveren, N. J., Bruggeman, R., Cahn, W., de Haan, L., Delespaul, P., Meijer, C. J., Myin-Germeys, I., Kahn, R. S., Schirmbeck, F., Simons, C. J. P., van Haren, N. E. M., & van Winkel, R. (2018). Childhood adversities and psychotic symptoms: The potential mediating or moderating role of neurocognition and social cognition. *Schizophrenia Research*. https://doi.org/10.1016/j.schres.2018.11.028

March, D., Hatch, S. L., Morgan, C., Kirkbride, J. B., Bresnahan, M., Fearon, P., & Susser, E. (2008). Psychosis and Place. *Epidemiologic Reviews*, *30*(1), 84–100. https://doi.org/10.1093/epirev/mxn006

Maric, N., Krabbendam, L., Vollebergh, W., de Graaf, R., & van Os, J. (2003). Sex differences in symptoms of psychosis in a non-selected, general population sample. *Schizophrenia Research*, *63*(1–2), 89–95. https://doi.org/10.1016/S0920-9964(02)00380-8

Marsh, H. W., Nagengast, B., Morin, A., J. S., re, Parada, R. H., Craven, R. G., & Hamilton, L. R. (2011). Construct validity of the multidimensional structure of bullying and victimization: An application of exploratory structural equation modeling. *Journal of Educational Psychology*, *103*(3), 701–732.

Martin, J. A., & Penn, D. L. (2002). Attributional Style in Schizophrenia: An Investigation in Outpatients With and Without Persecutory Delusions. *Schizophrenia Bulletin*, *28*(1), 131–141. https://doi.org/10.1093/oxfordjournals.schbul.a006916

Martin, J., Hamshere, M. L., Stergiakouli, E., O'Donovan, M. C., & Thapar, A. (2015). Neurocognitive abilities in the general population and composite genetic risk scores for attention-deficit hyperactivity disorder. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *56*(6), 648–656. https://doi.org/10.1111/jcpp.12336

McCutcheon, R. A., Bloomfield, M. A. P., Dahoun, T., Mehta, M., & Howes, O. D. (2018). Chronic psychosocial stressors are associated with alterations in salience processing and corticostriatal connectivity. *Schizophrenia Research*. https://doi.org/10.1016/j.schres.2018.12.011

McEwen, B. S., Bowles, N. P., Gray, J. D., Hill, M. N., Hunter, R. G., Karatsoreos, I. N., & Nasca, C. (2015). Mechanisms of stress in the brain. *Nature Neuroscience*, *18*(10), 1353–1363. https://doi.org/10.1038/nn.4086

McGrath, J. J., McLaughlin, K. A., Saha, S., Aguilar-Gaxiola, S., Al-Hamzawi, A., Alonso, J., Bruffaerts, R., de Girolamo, G., de Jonge, P., Esan, O., Florescu, S., Gureje, O., Haro, J. M., Hu, C., Karam, E. G., Kovess-Masfety, V., Lee, S., Lepine, J. P., Lim, C. C. W., … Kessler, R. C. (2017). The association between childhood adversities and subsequent first onset of psychotic experiences: A cross-national analysis of 23 998 respondents from 17 countries. *Psychological Medicine*, 1–16. https://doi.org/10.1017/S0033291716003263

McGrath, J., Saha, S., Chant, D., & Welham, J. (2008). Schizophrenia: A Concise Overview of Incidence, Prevalence, and Mortality. *Epidemiologic Reviews*, *30*(1), 67–76. https://doi.org/10.1093/epirev/mxn001

McGrath, Saha, S., Al-Hamzawi, A., Alonso, J., Bromet, E. J., Bruffaerts, R., Caldas-de-Almeida, J. M., Chiu, W. T., Jonge, P. de, Fayyad, J., Florescu, S., Gureje, O., Haro, J. M., Hu, C., Kovess-Masfety, V., Lepine, J. P., Lim, C. C. W., Mora, M. E. M., Navarro-Mateu, F., … Kessler, R. C. (2015). Psychotic Experiences in the General Population: A Cross-National Analysis Based on 31 261 Respondents From 18 Countries. *JAMA Psychiatry*, *72*(7), 697–705. https://doi.org/10.1001/jamapsychiatry.2015.0575

McGrath, Saha, S., Al-Hamzawi, A., Andrade, L., Benjet, C., Bromet, E. J., Browne, M. O., Caldas de Almeida, J. M., Chiu, W. T., Demyttenaere, K., Fayyad, J., Florescu, S., de Girolamo, G., Gureje, O., Haro, J. M., ten Have, M., Hu, C., Kovess-Masfety, V., Lim, C. C. W., … Kessler, R. C. (2016). The Bidirectional Associations Between Psychotic Experiences and DSM-IV Mental Disorders. *American Journal of Psychiatry*, *173*(10), 997–1006. https://doi.org/10.1176/appi.ajp.2016.15101293

McGrath, Saha, S., Lim, C. C. W., Aguilar-Gaxiola, S., Alonso, J., Andrade, L. H., Bromet, E. J., Bruffaerts, R., Caldas de Almeida, J. M., Cardoso, G., de Girolamo, G., Fayyad, J., Florescu, S., Gureje, O., Haro, J. M., Kawakami, N., Koenen, K. C., Kovess-Masfety, V., Lee, S., … Kessler, R. C. (2017). Trauma and psychotic experiences: Transnational data from the World Mental Health Survey. *The British Journal of Psychiatry*, *211*(6), 373–380. https://doi.org/10.1192/bjp.bp.117.205955

McKay, R., Langdon, R., & Coltheart, M. (2007). Jumping to delusions? Paranoia, probabilistic reasoning, and need for closure. *Cognitive Neuropsychiatry*, *12*(4), 362–376. https://doi.org/10.1080/13546800701203769

McLean, B. F., Mattiske, J. K., & Balzan, R. P. (2017). Association of the Jumping to Conclusions and Evidence Integration Biases With Delusions in Psychosis: A Detailed Meta-analysis. *Schizophrenia Bulletin*, *43*(2), 344–354. https://doi.org/10.1093/schbul/sbw056

McNally, R. J., Clancy, S. A., Barrett, H. M., & Parker, H. A. (2005). Reality monitoring in adults reporting repressed, recovered, or continuous memories of childhood sexual abuse. *Journal of Abnormal Psychology*, *114*(1), 147–152. https://doi.org/10.1037/0021-843X.114.1.147

Menard, C. B., Bandeen-Roche, K. J., & Chilcoat, H. D. (2004). Epidemiology of multiple childhood traumatic events: Child abuse, parental psychopathology, and other family-level stressors. *Social Psychiatry and Psychiatric Epidemiology*, *39*(11), 857–865. https://doi.org/10.1007/s00127-004-0868-8

Millier, A., Schmidt, U., Angermeyer, M. C., Chauhan, D., Murthy, V., Toumi, M., & Cadi-Soussi, N. (2014). Humanistic burden in schizophrenia: A literature review. *Journal of Psychiatric Research*, *54*, 85–93. https://doi.org/10.1016/j.jpsychires.2014.03.021

Miquel Porta (ed.). (2014). *Dictionary of Epidemiology* (6th ed.). Oxford University Press.

Misra, S., Gelaye, B., Koenen, K. C., Williams, D. R., Borba, C. P. C., Quattrone, D., Di Forti, M., La Cascia, C., La Barbera, D., Tarricone, I., Berardi, D., Szöke, A., Arango, C., Tortelli, A., de Haan, L., Velthorst, E., Bobes, J., Bernardo, M., Sanjuán, J., … Morgan, C. (2019). Early Parental Death and Risk of Psychosis in Offspring: A Six-Country Case-Control Study. *Journal of Clinical Medicine*, *8*(7), 1081. https://doi.org/10.3390/jcm8071081

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & Group, T. P. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLOS Medicine*, *6*(7), e1000097. https://doi.org/10.1371/journal.pmed.1000097

Mohr, C., & Ettinger, U. (2014). An Overview of the Association between Schizotypy and Dopamine. *Frontiers in Psychiatry*, *5*. https://doi.org/10.3389/fpsyt.2014.00184

Møller, P. (2000). The Initial Prodrome in Schizophrenia: Searching for Naturalistic Core Dimensions of Experience and Behavior. *Schizophrenia Bulletin*, *26*(1), 217–232.

Moore, T. H. M., Zammit, S., Lingford-Hughes, A., Barnes, T. R. E., Jones, P. B., Burke, M., & Lewis, G. (2007). Cannabis use and risk of psychotic or affective mental health outcomes: A systematic review. *Lancet (London, England)*, *370*(9584), 319–328. https://doi.org/10.1016/S0140-6736(07)61162-3

Moran, P. B., & Eckenrode, J. (1992). Protective personality characteristics among adolescent victims of maltreatment. *Child Abuse & Neglect*, *16*(5), 743–754. https://doi.org/10.1016/0145-2134(92)90111-4

Morgan, C., & Gayer-Anderson, C. (2016). Childhood adversities and psychosis: Evidence, challenges, implications. *World Psychiatry*, *15*(2), 93–102. https://doi.org/10.1002/wps.20330

Moritz S, Göritz AS, Balzan RP, Gawęda Ł, Kulagin SC, & Andreou C. (2017). A new paradigm to measure probabilistic reasoning and a possible answer to the question why psychosis-prone individuals jump to conclusions. *Journal of Abnormal Psychology*, *126*(4), 406–415. https://doi.org/10.1037/abn0000262

Moritz, S., Kerstan, A., Veckenstedt, R., Randjbar, S., Vitzthum, F., Schmidt, C., Heise, M., & Woodward, T. S. (2011). Further evidence for the efficacy of a metacognitive group training in schizophrenia. *Behaviour Research and Therapy*, *49*(3), 151–157. https://doi.org/10.1016/j.brat.2010.11.010

Moritz, Steffen, Köther, U., Hartmann, M., & Lincoln, T. M. (2015). Stress is a bad advisor. Stress primes poor decision making in deluded psychotic patients. *European Archives of Psychiatry and Clinical Neuroscience*, *265*(6), 461–469. https://doi.org/10.1007/s00406-015-0585-1

Moritz, Steffen, Scheu, F., Andreou, C., Pfueller, U., Weisbrod, M., & Roesch-Ely, D. (2016). Reasoning in psychosis: Risky but not necessarily hasty. *Cognitive Neuropsychiatry*, 1–16. https://doi.org/10.1080/13546805.2015.1136611

Moriyama, T. S., Drukker, M., Gadelha, A., Pan, P. M., Salum, G. A., Manfro, G. G., Mari, J. de J., Miguel, E. C., Rohde, L. A., Polanczyk, G. V., Os, J. van, & Bressan, R. A. (2018). The association between psychotic experiences and traumatic life events: The role of the intention to harm. *Psychological Medicine*, 1–12. https://doi.org/10.1017/S0033291717003762

Moutoussis, M., Bentall, R. P., El-Deredy, W., & Dayan, P. (2011). Bayesian modelling of Jumping-to-Conclusions bias in delusional patients. *Cognitive Neuropsychiatry*, *16*(5), 422–447. https://doi.org/10.1080/13546805.2010.548678

Moyer, D. M., DiPietro, L., Berkowitz, R. I., & Stunkard, A. J. (1997a). Childhood sexual abuse and precursors of binge eating in an adolescent female population. *The International Journal of Eating Disorders*, *21*(1), 23–30.

Moyer, D. M., DiPietro, L., Berkowitz, R. I., & Stunkard, A. J. (1997b). Childhood sexual abuse and precursors of binge eating in an adolescent female population. *The International Journal of Eating Disorders*, *21*(1), 23–30.

Muenzenmaier, K. H., Seixas, A. A., Schneeberger, A. R., Castille, D. M., Battaglia, J., & Link, B. G. (2015). Cumulative Effects of Stressful Childhood Experiences on Delusions and Hallucinations. *Journal of Trauma & Dissociation*, *16*(4), 442–462. https://doi.org/10.1080/15299732.2015.1018475

Murray, R M, & Lewis, S. W. (1987). Is schizophrenia a neurodevelopmental disorder? *British Medical Journal (Clinical Research Ed.)*, *295*(6600), 681–682.

Murray, Robin M., Bhavsar, V., Tripoli, G., & Howes, O. (2017). 30 Years on: How the Neurodevelopmental Hypothesis of Schizophrenia Morphed Into the Developmental Risk Factor Model of Psychosis. *Schizophrenia Bulletin*, *43*(6), 1190–1196. https://doi.org/10.1093/schbul/sbx121

Murray Straus, R. G., & Christine Smith. (1990). *Physical violence in American families: Risk factors and adaptations to violence in 8,145 families*. Transaction.

National Institute for Health Care Excellence. (2018). *Post-traumatic stress disorder*. https://www.nice.org.uk/guidance/ng116

Newbury, J., Arseneault, L., Caspi, A., Moffitt, T. E., Odgers, C. L., & Fisher, H. L. (2016). Why Are Children in Urban Neighborhoods at Increased Risk for Psychotic Symptoms? Findings From a UK Longitudinal Cohort Study. *Schizophrenia Bulletin*, *42*(6), 1372–1383. https://doi.org/10.1093/schbul/sbw052

Newbury, J. B., Arseneault, L., Beevers, S., Kitwiroon, N., Roberts, S., Pariante, C. M., Kelly, F. J., & Fisher, H. L. (2019). Association of Air Pollution Exposure With Psychotic Experiences During Adolescence. *JAMA Psychiatry*, *76*(6), 614–623. https://doi.org/10.1001/jamapsychiatry.2019.0056

Newson, R. (2015). *PUNAF: Stata module to compute population attributable fractions for cohort studies*. Boston College Department of Economics. https://ideas.repec.org/c/boc/bocode/s457193.html

NHS Education for Scotland. (2017). *Transforming Psychological Trauma: A Knowledge and Skills Framework for the Scottish Workforce*. https://www.nes.scot.nhs.uk/media/3971582/nationaltraumatrainingframework.pdf

Nierop, Martine van, Lecei, A., Myin-Germeys, I., Collip, D., Viechtbauer, W., Jacobs, N., Derom, C., Thiery, E., Os, J. van, & Winkel, R. van. (2018). Stress reactivity links childhood trauma exposure to an admixture of depressive, anxiety, and psychosis symptoms. *Psychiatry Research*, *260*, 451–457. https://doi.org/10.1016/j.psychres.2017.12.012

Norman, R. E., Byambaa, M., De, R., Butchart, A., Scott, J., & Vos, T. (2012). The Long-Term Health Consequences of Child Physical Abuse, Emotional Abuse, and Neglect: A Systematic Review and Meta-Analysis. *PLoS Medicine*, *9*(11), e1001349. https://doi.org/10.1371/journal.pmed.1001349

Nowicki, S. (2016). *Choice or Chance: Understanding your locus of control and why it matters*. Prometheus. https://www.researchgate.net/publication/311510916_Choice_or_Chance_Understanding_your_locus_of_control_and_why_it_matters

Ochoa, S., Haro, J. M., Huerta-Ramos, E., Cuevas-Esteban, J., Stephan-Otto, C., Usall, J., Nieto, L., & Brebion, G. (2014). Relation between jumping to conclusions and cognitive functioning in people with schizophrenia in contrast with healthy participants. *Schizophrenia Research*, *159*(1), 211–217. https://doi.org/10.1016/j.schres.2014.07.026

Ormrod, J., Shaftoe, D., Cavanagh, K., Freeston, M., Turkington, D., Price, J., & Dudley, R. (2012). A pilot study exploring the contribution of working memory to "jumping to conclusions" in people with first episode psychosis. *Cognitive Neuropsychiatry*, *17*(2), 97–114. https://doi.org/10.1080/13546805.2011.569372

Ouzzani, M., Hammady, H., Fedorowicz, Z., & Elmagarmid, A. (2016). Rayyan—A web and mobile app for systematic reviews. *Systematic Reviews*, *5*(1). https://doi.org/10.1186/s13643-016-0384-4

Owen, M. J., & O'Donovan, M. C. (2017). Schizophrenia and the neurodevelopmental continuum:evidence from genomics. *World Psychiatry: Official Journal of the World Psychiatric Association (WPA)*, *16*(3), 227–235. https://doi.org/10.1002/wps.20440

Pardiñas, A. F., Holmans, P., Pocklington, A. J., Escott-Price, V., Ripke, S., Carrera, N., Legge, S. E., Bishop, S., Cameron, D., Hamshere, M. L., Han, J., Hubbard, L., Lynham, A., Mantripragada, K., Rees, E., MacCabe, J. H., McCarroll, S. A., Baune, B. T., Breen, G., … Walters, J. T. R. (2018). Common schizophrenia alleles are enriched in mutation-intolerant genes and in regions under strong background selection. *Nature Genetics*, *50*(3), 381–389. https://doi.org/10.1038/s41588-018-0059-2

Park, H. Y., Bang, M., Kim, K. R., Lee, E., & An, S. K. (2018). Fragile Self and Malevolent Others: Biased Attribution Styles in Individuals at Ultra-High Risk for Psychosis. *Psychiatry Investigation*, *15*(8), 796–804. https://doi.org/10.30773/pi.2018.05.08

Pearson, R. M., Heron, J., Button, K., Bentall, R. P., Fernyhough, C., Mahedy, L., Bowes, L., & Lewis, G. (2015). *Cognitive styles and future depressed mood in early adulthood:the importance of global attributions*. http://opus.bath.ac.uk/47151/1/Published_Version.pdf

Pechtel, P., Lyons-Ruth, K., Anderson, C. M., & Teicher, M. H. (2014). Sensitive periods of amygdala development: The role of maltreatment in preadolescence. *NeuroImage*, *97*, 236–244. https://doi.org/10.1016/j.neuroimage.2014.04.025

Pechtel, P., & Pizzagalli, D. A. (2013). Disrupted Reinforcement Learning and Maladaptive Behavior in Women With a History of Childhood Sexual Abuse: A High-Density Event-Related Potential Study. *JAMA Psychiatry*, *70*(5), 499–507. https://doi.org/10.1001/jamapsychiatry.2013.728

Perälä, J., Suvisaari, J., Saarni, S. I., Kuoppasalmi, K., Isometsä, E., Pirkola, S., Partonen, T., Tuulio-Henriksson, A., Hintikka, J., Kieseppä, T., Härkänen, T., Koskinen, S., & Lönnqvist, J. (2007). Lifetime Prevalence of Psychotic and Bipolar I Disorders in a General Population. *Archives of General Psychiatry*, *64*(1), 19–28. https://doi.org/10.1001/archpsyc.64.1.19

Pereda, N., Guilera, G., Forns, M., & Gómez-Benito, J. (2009). The prevalence of child sexual abuse in community and student samples: A meta-analysis. *Clinical Psychology Review*, *29*(4), 328–338. https://doi.org/10.1016/j.cpr.2009.02.007

Perry, B. D., Pollard, R. A., Blakley, T. L., Baker, W. L., & Vigilante, D. (1995). Childhood trauma, the neurobiology of adaptation, and "use-dependent" development of the brain: How "states" become "traits". *Infant Mental Health Journal*, *16*(4), 271–291. https://doi.org/10.1002/1097-0355(199524)16:4<271::AID-IMHJ2280160404>3.0.CO;2-B

Peters, E., & Garety, P. (2006). Cognitive functioning in delusions: A longitudinal analysis. *Behaviour Research and Therapy*, *44*(4), 481–514. https://doi.org/10.1016/j.brat.2005.03.008

Peters, E., Joseph, S., Day, S., & Garety, P. (2004). Measuring Delusional Ideation: The 21-Item Peters et al. Delusions Inventory (PDI). *Schizophrenia Bulletin*, *30*(4), 1005–1022.

Peterson, C., Semmel, A., Baeyer, C. von, Abramson, L. Y., Metalsky, G. I., & Seligman, M. E. P. (1982). The attributional Style Questionnaire. *Cognitive Therapy and Research*, *6*(3), 287–299. https://doi.org/10.1007/BF01173577

Pos, K., Meijer, C. J., Verkerk, O., Ackema, O., Krabbendam, L., & de Haan, L. (2018). Metacognitive training in patients recovering from a first psychosis: An experience sampling study testing treatment effects. *European Archives of Psychiatry and Clinical Neuroscience*, *268*(1), 57–64. https://doi.org/10.1007/s00406-017-0833-7

Pot-Kolder, R., Veling, W., Counotte, J., & van der Gaag, M. (2018). Self-reported Cognitive Biases Moderate the Associations Between Social Stress and Paranoid Ideation in a Virtual Reality Experimental Study. *Schizophrenia Bulletin*. https://doi.org/10.1093/schbul/sbx119

Pouget, J. G., Han, B., Wu, Y., Mignot, E., Ollila, H. M., Barker, J., Spain, S., Dand, N., Trembath, R., Martin, J., Mayes, M. D., Bossini-Castillo, L., López-Isac, E., Jin, Y., Santorico, S. A., Spritz, R. A., Hakonarson, H., Polychronakos, C., Raychaudhuri, S., & Knight, J. (2019). Cross-disorder analysis of schizophrenia and 19 immune-mediated diseases identifies shared genetic risk. *Human Molecular Genetics*. https://doi.org/10.1093/hmg/ddz145

Prabhu, V. V., Nguyen, T. B., Cui, Y., Oh, Y.-E., Lee, K.-H., Bagalkot, T. R., & Chung, Y.-C. (2018). Effects of social defeat stress on dopamine D2 receptor isoforms and proteins involved in intracellular trafficking. *Behavioral and Brain Functions*, *14*(1), 16. https://doi.org/10.1186/s12993-018-0148-5

Premkumar, P., Cooke, M. A., Fannon, D., Peters, E., Michel, T. M., Aasen, I., Murray, R. M., Kuipers, E., & Kumari, V. (2008). Misattribution bias of threat-related facial expressions is related to a longer duration of illness and poor executive function in schizophrenia and schizoaffective disorder. *European Psychiatry*, *23*(1), 14–19. https://doi.org/10.1016/j.eurpsy.2007.10.004

Psychotic Experiences and Psychotic Disorders at Age 18 in Relation to Psychotic Experiences at Age 12 in a Longitudinal Population-Based Cohort Study. (2013). *American Journal of Psychiatry*, *170*(7), 742–750. https://doi.org/10.1176/appi.ajp.2013.12060768

Pulcu, E., & Browning, M. (2017). Affective bias as a rational response to the statistics of rewards and punishments. *ELife*, *6*, e27879. https://doi.org/10.7554/eLife.27879

Radford, L., Corral, S., Bradley, C., & Fisher, H. L. (2013). The prevalence and impact of child maltreatment and other types of victimization in the UK: Findings from a population survey of caregivers, children and young people and young adults. *Child Abuse & Neglect*, *37*(10), 801–813. https://doi.org/10.1016/j.chiabu.2013.02.004

Radliff, K. M., Wang, C., & Swearer, S. M. (2016). Bullying and Peer Victimization: An Examination of Cognitive and Psychosocial Constructs. *Journal of Interpersonal Violence*, *31*(11), 1983–2005.

Reichenberg, A. (2005). Cognitive impairment as a risk factor for psychosis. *Dialogues in Clinical Neuroscience*, *7*(1), 31–38.

Reininghaus, U., Rauschenberg, C., Ten Have, M., de Graaf, R., van Dorsselaer, S., Simons, C. J. P., Gunther, N., Pries, L.-K., Guloksuz, S., Radhakrishnan, R., Bak, M., & van Os, J. (2018). Reasoning bias, working memory performance and a transdiagnostic phenotype of affective disturbances and psychotic experiences in the general population. *Psychological Medicine*, 1–11. https://doi.org/10.1017/S0033291718002209

Rhodes, J. E., Fischer, K., Ebert, L., & Meyers, A. B. (1993). Patterns of service utilization among pregnant and parenting African American adolescents. *Psychology of Women Quarterly*, *17*(3), 257–274.

Roazzi, A., Attili, G., Pentima, L. D., & Toni, A. (2016). Locus of control in maltreated children: The impact of attachment and cumulative trauma. *Psicologia: Reflexão e Crítica*, *29*(1), 8. https://doi.org/10.1186/s41155-016-0025-9

Rodier, M., Prévost, M., Renoult, L., Lionnet, C., Kwann, Y., Dionne-Dostie, E., Chapleau, I., & Debruille, J. B. (2011). Healthy people with delusional ideation change their mind with conviction. *Psychiatry Research*, *189*(3), 433–439. https://doi.org/10.1016/j.psychres.2011.06.018

Rodriguez, V., Ajnakina, O., Stilo, S. A., Mondelli, V., Marques, T. R., Trotta, A., Quattrone, D., Gardner-Sood, P., Colizzi, M., Wiffen, B. D., Dazzan, P., Forti, M. D., Falcone, M. A., David, A. S., & Murray, R. M. (2018). Jumping to conclusions at first onset of psychosis predicts longer admissions, more compulsory admissions and police involvement over the next 4 years: The GAP study. *Psychological Medicine*, 1–11. https://doi.org/10.1017/S0033291718003197

Rogosch, F. A., Dackis, M. N., & Cicchetti, D. (2011). Child Maltreatment and Allostatic Load: Consequences for Physical and Mental Health in Children from Low-Income Families. *Development and Psychopathology*, *23*(4), 1107–1124. https://doi.org/10.1017/S0954579411000587

Roiser, J. P., Howes, O. D., Chaddock, C. A., Joyce, E. M., & McGuire, P. (2013). Neural and Behavioral Correlates of Aberrant Salience in Individuals at Risk for Psychosis. *Schizophrenia Bulletin*, *39*(6), 1328–1336. https://doi.org/10.1093/schbul/sbs147

Rolls, E. T., Loh, M., Deco, G., & Winterer, G. (2008). Computational models of schizophrenia and dopamine modulation in the prefrontal cortex. *Nature Reviews. Neuroscience*, *9*(9), 696–709. https://doi.org/10.1038/nrn2462

Ross, K., Freeman, D., Dunn, G., & Garety, P. (2011). A Randomized Experimental Investigation of Reasoning Training for People With Delusions. *Schizophrenia Bulletin*, *37*(2), 324–333. https://doi.org/10.1093/schbul/sbn165

Ross, McKay, R., Coltheart, M., & Langdon, R. (2015). Jumping to Conclusions About the Beads Task? A Meta-analysis of Delusional Ideation and Data-Gathering. *Schizophrenia Bulletin*, *41*(5), 1183–1191. https://doi.org/10.1093/schbul/sbu187

Ross, R. M., Pennycook, G., McKay, R., Gervais, W. M., Langdon, R., & Coltheart, M. (2016). Analytic cognitive style, not delusional ideation, predicts data gathering in a large beads task study. *Cognitive Neuropsychiatry*, 1–15. https://doi.org/10.1080/13546805.2016.1192025

Royston, P. (2004). Multiple Imputation of Missing Values. *The Stata Journal*, *4*(3), 227–241. https://doi.org/10.1177/1536867X0400400301

Rucklidge, J. J., Brown, D. L., Crawford, S., & Kaplan, B. J. (2016a). Retrospective reports of childhood trauma in adults with ADHD. *Journal of Attention Disorders*, *9*(4), 631–641.

Rucklidge, J. J., Brown, D. L., Crawford, S., & Kaplan, B. J. (2016b). Retrospective reports of childhood trauma in adults with ADHD. *Journal of Attention Disorders*, *9*(4), 631–641.

S. Sharp, P. K. S. (1994). Understanding bullying. In *Tackling bullying in your school: A practical handbook for teachers*. Routledge.

Sareen, J., Cox, B. J., Goodwin, R. D., & Asmundson, G. J. G. (2005). Co-occurrence of posttraumatic stress disorder with positive psychotic symptoms in a nationally representative sample. *Journal of Traumatic Stress*, *18*(4), 313–322. https://doi.org/10.1002/jts.20040

Saridjan, N. S., Huizink, A. C., Koetsier, J. A., Jaddoe, V. W., Mackenbach, J. P., Hofman, A., Kirschbaum, C., Verhulst, F. C., & Tiemeier, H. (2010). Do social disadvantage and early family adversity affect the diurnal cortisol rhythm in infants? The Generation R Study. *Hormones and Behavior*, *57*(2), 247–254. https://doi.org/10.1016/j.yhbeh.2009.12.001

Saunders, B. E., & Adams, Z. W. (2014). Epidemiology of Traumatic Experiences in Childhood. *Child and Adolescent Psychiatric Clinics of North America*, *23*(2), 167–184. https://doi.org/10.1016/j.chc.2013.12.003

Savransky, A., Chiappelli, J., Fisseha, F., Wisner, K. M., Xiaoming, D., Mirmomen, S. M., Jones, A. D., Adhikari, B. M., Bruce, H. A., Rowland, L. M., & Hong, L. E. (2018). Elevated allostatic load early in the course of schizophrenia. *Translational Psychiatry*, *8*(1), 246. https://doi.org/10.1038/s41398-018-0299-z

Sayal, K., Heron, J., Maughan, B., Rowe, R., & Ramchandani, P. (2014). Infant temperament and childhood psychiatric disorder: Longitudinal study. *Child: Care Health and Development*, *40*(2), 292–297. https://doi.org/10.1111/cch.12054

Schalinski, I., Breinlinger, S., Hirt, V., Teicher, M. H., Odenwald, M., & Rockstroh, B. (2017). Environmental adversities and psychotic symptoms: The impact of timing of trauma, abuse, and neglect. *Schizophrenia Research*. https://doi.org/10.1016/j.schres.2017.10.034

Schmack, K., Castro, A. G.-C. de, Rothkirch, M., Sekutowicz, M., Rössler, H., Haynes, J.-D., Heinz, A., Petrovic, P., & Sterzer, P. (2013). Delusions and the Role of Beliefs in Perceptual Inference. *Journal of Neuroscience*, *33*(34), 13701–13712. https://doi.org/10.1523/JNEUROSCI.1778-13.2013

Schmack, K., Schnack, A., Priller, J., & Sterzer, P. (2015). Perceptual instability in schizophrenia: Probing predictive coding accounts of delusions with ambiguous stimuli. *Schizophrenia Research: Cognition*, *2*(2), 72–77. https://doi.org/10.1016/j.scog.2015.03.005

Schoeler, T., Choi, S. W., Dudbridge, F., Baldwin, J., Duncan, L., Cecil, C. M., Walton, E., Viding, E., McCrory, E., & Pingault, J.-B. (2019). Multi-Polygenic Score Approach to Identifying Individual Vulnerabilities Associated With the Risk of Exposure to Bullying. *JAMA Psychiatry*, *76*(7), 730–738. https://doi.org/10.1001/jamapsychiatry.2019.0310

Schofield, P., Thygesen, M., Das-Munshi, J., Becares, L., Cantor-Graae, E., Agerbo, E., & Pedersen, C. (2018). Neighbourhood ethnic density and psychosis—Is there a difference according to generation? *Schizophrenia Research*, *195*, 501–505. https://doi.org/10.1016/j.schres.2017.09.029

Schreier, A., Wolke, D., Thomas, K., Horwood, J., Hollis, C., Gunnell, D., Lewis, G., Thompson, A., Zammit, S., Duffy, L., Salvi, G., & Harrison, G. (2009). Prospective Study of Peer Victimization in Childhood and Psychotic Symptoms in a Nonclinical Population at Age 12 Years. *Archives of General Psychiatry*, *66*(5), 527–536. https://doi.org/10.1001/archgenpsychiatry.2009.23

Schroeder, A., Notaras, M., Du, X., & Hill, R. A. (2018). On the Developmental Timing of Stress: Delineating Sex-Specific Effects of Stress across Development on Adult Behavior. *Brain Sciences*, *8*(7). https://doi.org/10.3390/brainsci8070121

Seeman, P., Lee, T., Chau-Wong, M., & Wong, K. (1976). Antipsychotic drug doses and neuroleptic/dopamine receptors. *Nature*, *261*(5562), 717. https://doi.org/10.1038/261717a0

Seligman, M. E., & al, et. (1984). Attributional style and depressive symptoms among children. *Journal of Abnormal Psychology*, *93*(2), 235–238.

Selten, J.-P., & Cantor-Graae, E. (2005). Social defeat: Risk factor for schizophrenia? *The British Journal of Psychiatry*, *187*(2), 101–102. https://doi.org/10.1192/bjp.187.2.101

Selten, J.-P., Ven, E. van der, Rutten, B. P. F., & Cantor-Graae, E. (2013). The Social Defeat Hypothesis of Schizophrenia: An Update. *Schizophrenia Bulletin*, *39*(6), 1180–1186. https://doi.org/10.1093/schbul/sbt134

Sharifi, V., Eaton, W. W., Wu, L. T., Roth, K. B., Burchett, B. M., & Mojtabai, R. (2015). Psychotic experiences and risk of death in the general population: 24–27 year follow-up of the Epidemiologic Catchment Area study. *The British Journal of Psychiatry*, *207*(1), 30–36. https://doi.org/10.1192/bjp.bp.113.143198

Shevlin, M., Houston, J. E., Dorahy, M. J., & Adamson, G. (2008). Cumulative Traumas and Psychosis: An Analysis of the National Comorbidity Survey and the British Psychiatric Morbidity Survey. *Schizophrenia Bulletin*, *34*(1), 193–199. https://doi.org/10.1093/schbul/sbm069

Shevlin, M., O'Neill, T., Houston, J. E., Read, J., Bentall, R. P., & Murphy, J. (2013). Patterns of lifetime female victimisation and psychotic experiences: A study based on the UK Adult Psychiatric Morbidity Survey 2007. *Social Psychiatry and Psychiatric Epidemiology*, *48*(1), 15–24. https://doi.org/10.1007/s00127-012-0573-y

Shonkoff, J. P., Boyce, W. T., & McEwen, B. S. (2009). Neuroscience, molecular biology, and the childhood roots of health disparities: Building a new framework for health promotion and disease prevention. *JAMA*, *301*(21), 2252–2259. https://doi.org/10.1001/jama.2009.754

So, & Kwok, N. T. (2015). Jumping to Conclusions Style along the Continuum of Delusions: Delusion-Prone Individuals Are Not Hastier in Decision Making than Healthy Individuals. *PLOS ONE*, *10*(3), e0121347. https://doi.org/10.1371/journal.pone.0121347

So, S. H., Freeman, D., Dunn, G., Kapur, S., Kuipers, E., Bebbington, P., Fowler, D., & Garety, P. A. (2012). Jumping to Conclusions, a Lack of Belief Flexibility and Delusional Conviction in Psychosis. *Journal of Abnormal Psychology*, *121*(1), 129–139. https://doi.org/10.1037/a0025297

So, S. H.-W., Chan, A. P., Chong, C. S.-Y., Wong, M. H.-M., Lo, W. T.-L., Chung, D. W.-S., & Chan, S. S. (2015). Metacognitive training for delusions (MCTd): Effectiveness on data-gathering and belief flexibility in a Chinese sample. *Frontiers in Psychology*, *6*. https://doi.org/10.3389/fpsyg.2015.00730

So, Siu, N. Y.-F., Wong, H.-L., Chan, W., & Garety, P. A. (2016). 'Jumping to conclusions' data-gathering bias in psychosis and other psychiatric disorders—Two meta-analyses of comparisons between patients and healthy individuals. *Clinical Psychology Review*, *46*, 151–167. https://doi.org/10.1016/j.cpr.2016.05.001

Solberg, M. E., & Olweus, D. (2003). Prevalence estimation of school bullying with the Olweus Bully/Victim Questionnaire. *Aggressive Behavior*, *29*(3), 239–268. https://doi.org/10.1002/ab.10047

Solmi, F., Colman, I., Weeks, M., Lewis, G., & Kirkbride, J. B. (2017). Trajectories of Neighborhood Cohesion in Childhood, and Psychotic and Depressive Symptoms at Age 13 and 18 Years. *Journal of the American Academy of Child & Adolescent Psychiatry*, *56*(7), 570–577. https://doi.org/10.1016/j.jaac.2017.04.003

Spauwen, J., Krabbendam, L., Lieb, R., Wittchen, H. U., & Os, J. van. (2004). Early maternal stress and health behaviours and offspring expression of psychosis in adolescence. *Acta Psychiatrica Scandinavica*, *110*(5), 356–364. https://doi.org/10.1111/j.1600-0447.2004.00429.x

Spauwen, Janneke, Krabbendam, L., Lieb, R., Wittchen, H.-U., & Os, J. V. (2006). Impact of psychological trauma on the development of psychotic symptoms: Relationship with psychosis proneness. *The British Journal of Psychiatry*, *188*(6), 527–533. https://doi.org/10.1192/bjp.bp.105.011346

Speechley, W. J., Whitman, J. C., & Woodward, T. S. (2010). The contribution of hypersalience to the "jumping to conclusions" bias associated with delusions in schizophrenia. *Journal of Psychiatry & Neuroscience : JPN*, *35*(1), 7–17. https://doi.org/10.1503/jpn.090025

Stern, S. (1989). Rules of thumb for comparing multinomial logit and multinomial probit coefficients. *Economics Letters*, *31*(3), 235–238. https://doi.org/10.1016/0165-1765(89)90006-2

Sterne, J. A. C., White, I. R., Carlin, J. B., Spratt, M., Royston, P., Kenward, M. G., Wood, A. M., & Carpenter, J. R. (2009). Multiple imputation for missing data in epidemiological and clinical research: Potential and pitfalls. *The BMJ*, *338*. https://doi.org/10.1136/bmj.b2393

Sterne, J. A., & Davey Smith, G. (2001). Sifting the evidence-what's wrong with significance tests? *BMJ (Clinical Research Ed.)*, *322*(7280), 226–231.

Sterzer, P., Adams, R. A., Fletcher, P., Frith, C., Lawrie, S. M., Muckli, L., Petrovic, P., Uhlhaas, P., Voss, M., & Corlett, P. R. (2018). The Predictive Coding Account of Psychosis. *Biological Psychiatry*, *84*(9), 634–643. https://doi.org/10.1016/j.biopsych.2018.05.015

Sterzer, P., Voss, M., Schlagenhauf, F., & Heinz, A. (2018). Decision-making in schizophrenia: A predictive-coding perspective. *NeuroImage*. https://doi.org/10.1016/j.neuroimage.2018.05.074

Stoltenborgh, M., Bakermans-Kranenburg, M. J., Alink, L. R. A., & van IJzendoorn, M. H. (2015). The Prevalence of Child Maltreatment across the Globe: Review of a Series of Meta-Analyses. *Child Abuse Review*, *24*(1), 37–50. https://doi.org/10.1002/car.2353

Stover, C. S., Hahn, H., Im, J. J. Y., & Berkowitz, S. (2010). Agreement of Parent and Child Reports of Trauma Exposure and Symptoms in the Peritraumatic Period. *Psychological Trauma : Theory, Research, Practice and Policy*, *2*(3), 159–168a. https://doi.org/10.1037/a0019156

Stuke, H., Stuke, H., Weilnhammer, V. A., & Schmack, K. (2017). Psychotic Experiences and Overhasty Inferences Are Related to Maladaptive Learning. *PLoS Computational Biology*, *13*(1). https://doi.org/10.1371/journal.pcbi.1005328

Sullivan, S. A., Thompson, A., Kounali, D., Lewis, G., & Zammit, S. (2017). The longitudinal association between external locus of control, social cognition and adolescent psychopathology. *Social Psychiatry and Psychiatric Epidemiology*, *52*(6), 643–655. https://doi.org/10.1007/s00127-017-1359-z

Sullivan, S., Bentall, R. P., Fernyhough, C., Pearson, R. M., & Zammit, S. (2013). Cognitive Styles and Psychotic Experiences in a Community Sample. *PLOS ONE*, *8*(11), e80055. https://doi.org/10.1371/journal.pone.0080055

Swearer, S. M., Turner, R. K., Givens, J. E., & Pollack, W. S. (2008). 'You're so gay!': Do different forms of bullying matter for adolescent males? *School Psychology Review*, *37*(2), 160–173.

Takeda, T., Nakataki, M., Ohta, M., Hamatani, S., Matsuura, K., & Ohmori, T. (2018). Effect of cognitive function on jumping to conclusion in patients with schizophrenia. *Schizophrenia Research: Cognition*, *12*, 50–55. https://doi.org/10.1016/j.scog.2018.04.002

Teeple, R. C., Caplan, J. P., & Stern, T. A. (2009). Visual Hallucinations: Differential Diagnosis and Treatment. *Primary Care Companion to The Journal of Clinical Psychiatry*, *11*(1), 26–32.

Teufel, C., Subramaniam, N., Dobler, V., Perez, J., Finnemann, J., Mehta, P. R., Goodyer, I. M., & Fletcher, P. C. (2015). Shift toward prior knowledge confers a perceptual advantage in early psychosis and psychosis-prone healthy individuals. *Proceedings of the National Academy of Sciences*, *112*(43), 13401–13406. https://doi.org/10.1073/pnas.1503916112

Thomas, K., Harrison, G., Zammit, S., Lewis, G., Horwood, J., Heron, J., Hollis, C., Wolke, D., Thompson, A., & Gunnell, D. (2009). Association of measures of fetal and childhood growth with non-clinical psychotic symptoms in 12-year-olds: The ALSPAC cohort. *The British Journal of Psychiatry*, *194*(6), 521–526. https://doi.org/10.1192/bjp.bp.108.051730

Thompson, A. D., Nelson, B., Yuen, H. P., Lin, A., Amminger, G. P., McGorry, P. D., Wood, S. J., & Yung, A. R. (2013). Sexual Trauma Increases the Risk of Developing Psychosis in an Ultra High-Risk "Prodromal" Population. *Schizophrenia Bulletin*, sbt032. https://doi.org/10.1093/schbul/sbt032

Thompson, A., Sullivan, S., Lewis, G., Zammit, S., Heron, J., Horwood, J., Thomas, K., Gunnell, D., Hollis, C., Wolke, D., & Harrison, G. (2011). Association between locus of control in childhood and psychotic symptoms in early adolescence: Results from a large birth cohort. *Cognitive Neuropsychiatry*, *16*(5), 385–402. https://doi.org/10.1080/13546805.2010.546077

Thompson, R., Lewis, T., Neilson, E. C., English, D. J., Litrownik, A. J., Margolis, B., Proctor, L., & Dubowitz, H. (2017). Child Maltreatment and Risky Sexual Behavior: Indirect Effects Through Trauma Symptoms and Substance Use. *Child Maltreatment*, *22*(1), 69–78. https://doi.org/10.1177/1077559516674595

Thurber, S. (1977). Natural disaster and the dimensionality of the I-E scale. *The Journal of Social Psychology*, *103*(1), 159–160.

Tibshirani, R. (1996). Regression Shrinkage and Selection via the Lasso. *Journal of the Royal Statistical Society. Series B (Methodological)*, *58*(1), 267–288.

Tilling, K., Williamson, E. J., Spratt, M., Sterne, J. A. C., & Carpenter, J. R. (2016). Appropriate inclusion of interactions was needed to avoid bias in multiple imputation. *Journal of Clinical Epidemiology*, *80*, 107–115. https://doi.org/10.1016/j.jclinepi.2016.07.004

Tinghög, P., Malm, A., Arwidson, C., Sigvardsdotter, E., Lundin, A., & Saboonchi, F. (2017). Prevalence of mental ill health, traumas and postmigration stress among refugees from Syria resettled in Sweden after 2011: A population-based survey. *BMJ Open*, *7*(12). https://doi.org/10.1136/bmjopen-2017-018899

Toyoda, A. (2017). Social defeat models in animal science: What we have learned from rodent models. *Animal Science Journal = Nihon Chikusan Gakkaiho*, *88*(7), 944–952. https://doi.org/10.1111/asj.12809

Trauelsen, A. M., Bendall, S., Jansen, J. E., Nielsen, H.-G. L., Pedersen, M. B., Trier, C. H., Haahr, U. H., & Simonsen, E. (2015). Childhood adversity specificity and dose-response effect in non-affective first-episode psychosis. *Schizophrenia Research*, *165*(1), 52–59. https://doi.org/10.1016/j.schres.2015.03.014

Tripoli, G., Quattrone, D., Ferraro, L., Gayer-Anderson, C., Rodriguez, V., Cascia, C. L., Barbera, D. L., Sartorio, C., Seminerio, F., Tarricone, I., Berardi, D., Szöke, A., Arango, C., Tortelli, A., Llorca, P.-M., Haan, L. de, Velthorst, E., Bobes, J., Bernardo, M., … Forti, M. D. (2020). Jumping to conclusions, general intelligence, and psychosis liability: Findings from the multi-centre EU-GEI case-control study. *Psychological Medicine*, 1–11. https://doi.org/10.1017/S003329171900357X

Trotta, A., Murray, R. M., & Fisher, H. L. (2015). The impact of childhood adversity on the persistence of psychotic symptoms: A systematic review and meta-analysis. *Psychological Medicine*, *45*(12), 2481–2498. https://doi.org/10.1017/S0033291715000574

Ttofi, M. M., & Farrington, D. P. (2011). Effectiveness of school-based programs to reduce bullying: A systematic and meta-analytic review. *Journal of Experimental Criminology*, *7*(1), 27–56. https://doi.org/10.1007/s11292-010-9109-1

Unterrassner, L., Wyss, T. A., Wotruba, D., Haker, H., & Rössler, W. (2017). The Intricate Relationship between Psychotic-Like Experiences and Associated Subclinical Symptoms in Healthy Individuals. *Frontiers in Psychology*, *8*. https://doi.org/10.3389/fpsyg.2017.01537

Urbańska, D., Moritz, S., & Gawęda, Ł. (2019). The impact of social and sensory stress on cognitive biases and delusions in schizophrenia. *Cognitive Neuropsychiatry*, *24*(3), 217–232. https://doi.org/10.1080/13546805.2019.1611551

Van Dael, F., Versmissen, D., Janssen, I., Myin-Germeys, I., van Os, J., & Krabbendam, L. (2006). Data Gathering: Biased in Psychosis? *Schizophrenia Bulletin*, *32*(2), 341–351. https://doi.org/10.1093/schbul/sbj021

van den Berg, D. P. G., de Bont, P. A. J. M., van der Vleugel, B. M., de Roos, C., de Jongh, A., van Minnen, A., & van der Gaag, M. (2016). Trauma-Focused Treatment in PTSD Patients With Psychosis: Symptom Exacerbation, Adverse Events, and Revictimization. *Schizophrenia Bulletin*, *42*(3), 693–702. https://doi.org/10.1093/schbul/sbv172

van den Berg, D. P. G., & van der Gaag, M. (2012). Treating trauma in psychosis with EMDR: A pilot study. *Journal of Behavior Therapy and Experimental Psychiatry*, *43*(1), 664–671. https://doi.org/10.1016/j.jbtep.2011.09.011

van den Berg DG, de Bont PM, van der Vleugel BM, & et al. (2015). Prolonged exposure vs eye movement desensitization and reprocessing vs waiting list for posttraumatic stress disorder in patients with a psychotic disorder: A randomized clinical trial. *JAMA Psychiatry*, *72*(3), 259–267. https://doi.org/10.1001/jamapsychiatry.2014.2637

van der Put, C. E., Assink, M., Gubbels, J., & Boekhout van Solinge, N. F. (2018). Identifying Effective Components of Child Maltreatment Interventions: A Meta-analysis. *Clinical Child and Family Psychology Review*, *21*(2), 171–202. https://doi.org/10.1007/s10567-017-0250-5

van Nierop, M., van Os, J., Gunther, N., van Zelst, C., de Graaf, R., ten Have, M., van Dorsselaer, S., Bak, M., Myin-Germeys, I., & van Winkel, R. (2014). Does social defeat mediate the association between childhood trauma and psychosis? Evidence from the NEMESIS-2 Study. *Acta Psychiatrica Scandinavica*, *129*(6), 467–476. https://doi.org/10.1111/acps.12212

van Nierop, Martine, Lataster, T., Smeets, F., Gunther, N., van Zelst, C., de Graaf, R., ten Have, M., van Dorsselaer, S., Bak, M., Myin-Germeys, I., Viechtbauer, W., van Os, J., & van Winkel, R. (2014). Psychopathological Mechanisms Linking Childhood Traumatic Experiences to Risk of Psychotic Symptoms: Analysis of a Large, Representative Population-Based Sample. *Schizophrenia Bulletin*, *40*(Suppl_2), S123–S130. https://doi.org/10.1093/schbul/sbt150 van Os, J., Linscott, R. J., Myin-Germeys, I., Delespaul, P., & Krabbendam, L. (2009). A systematic review and meta-analysis of the psychosis continuum: Evidence for a psychosis proneness–persistence–impairment model of psychotic disorder. *Psychological Medicine*, *39*(02), 179. https://doi.org/10.1017/S0033291708003814

Varese, F., Smeets, F., Drukker, M., Lieverse, R., Lataster, T., Viechtbauer, W., Read, J., Os, J. van, & Bentall, R. P. (2012). Childhood Adversities Increase the Risk of Psychosis: A Meta-analysis of Patient-Control, Prospective- and Cross-sectional Cohort Studies. *Schizophrenia Bulletin*, *38*(4), 661–671. https://doi.org/10.1093/schbul/sbs050

Vassos, E., Pedersen, C. B., Murray, R. M., Collier, D. A., & Lewis, C. M. (2012). Meta-Analysis of the Association of Urbanicity With Schizophrenia. *Schizophrenia Bulletin*, *38*(6), 1118–1123. https://doi.org/10.1093/schbul/sbs096

Vlahovicova, K., Melendez-Torres, G. J., Leijten, P., Knerr, W., & Gardner, F. (2017). Parenting Programs for the Prevention of Child Physical Abuse Recurrence: A Systematic Review and Meta-Analysis. *Clinical Child and Family Psychology Review*, *20*(3), 351–365. https://doi.org/10.1007/s10567-017-0232-7

Walsh, K., Blaustein, M., Knight, W., Grant, a, Spinazzola, J., & van der Kolk, B. A. (2007). Resiliency factors in the relation between childhood sexual abuse and adulthood sexual assault in college-age women. *Journal of Child Sexual Abuse*, *16*(1), 1–17.

Waltz, J., Demro, C., Schiffman, J., Thompson, E., Kline, E., Reeves, G., Xu, Z., & Gold, J. (2015). Reinforcement learning performance and risk for psychosis in youth. *The Journal of Nervous and Mental Disease*, *203*(12), 919–926. https://doi.org/10.1097/NMD.0000000000000420

Ward, T., Peters, E., Jackson, M., Day, F., & Garety, P. A. (2018). Data-Gathering, Belief Flexibility, and Reasoning Across the Psychosis Continuum. *Schizophrenia Bulletin*. https://doi.org/10.1093/schbul/sbx029

Wasserstein, R. L., Schirm, A. L., & Lazar, N. A. (2019). Moving to a World Beyond “p < 0.05”. *The American Statistician*, *73*(sup1), 1–19. https://doi.org/10.1080/00031305.2019.1583913

Wells, G., Shea, B., Peterson J, Welch V, & Losos M. (2009). *The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses*. http://www.ohrica/programs/clinical_epidemiology/oxfordasp. 2009.

Wigman, J. T. W., van Winkel, R., Ormel, J., Verhulst, F. C., van Os, J., & Vollebergh, W. a. M. (2012). Early trauma and familial risk in the development of the extended psychosis phenotype in adolescence. *Acta Psychiatrica Scandinavica*, *126*(4), 266–273. https://doi.org/10.1111/j.1600-0447.2012.01857.x

Wigman, J. T. W., Winkel, R. van, Raaijmakers, Q. a. W., Ormel, J., Verhulst, F. C., Reijneveld, S. A., Os, J. van, & Vollebergh, W. a. M. (2011). Evidence for a persistent, environment-dependent and deteriorating subtype of subclinical psychotic experiences: A 6-year longitudinal general population study. *Psychological Medicine*, *41*(11), 2317–2329. https://doi.org/10.1017/S0033291711000304

Wilkinson, S., Dodgson, G., & Meares, K. (2017). Predictive Processing and the Varieties of Psychological Trauma. *Frontiers in Psychology*, *8*. https://doi.org/10.3389/fpsyg.2017.01840

Williams, J., Bucci, S., Berry, K., & Varese, F. (2018). Psychological mediators of the association between childhood adversities and psychosis: A systematic review. *Clinical Psychology Review*. https://doi.org/10.1016/j.cpr.2018.05.009

Winkel, R. van, Nierop, M. van, Myin-Germeys, I., & Os, J. van. (2013). Childhood Trauma as a Cause of Psychosis: Linking Genes, Psychology, and Biology. *The Canadian Journal of Psychiatry*, *58*(1), 44–51. https://doi.org/10.1177/070674371305800109

Winton-Brown, T. T., Broome, M. R., Allen, P., Valli, I., Howes, O., Garety, P. A., Johns, L. C., & McGuire, P. (2015). Misattributing speech and jumping to conclusions: A longitudinal study in people at high risk of psychosis. *European Psychiatry: The Journal of the Association of European Psychiatrists*, *30*(1), 32–37. https://doi.org/10.1016/j.eurpsy.2014.09.416

Wolfe, J., Kimerling, R.,. (1997). Gender issues in the assessment of posttraumatic stress disorder. In *Assessing Psychological Trauma and PTSD.* Guilford Press.

Wolke, D., Lereya, S. T., Fisher, H. L., Lewis, G., & Zammit, S. (2014). Bullying in elementary school and psychotic experiences at 18 years: A longitudinal, population-based cohort study. *Psychological Medicine*, *44*(10), 2199–2211. https://doi.org/10.1017/S0033291713002912

Wood, A. M., White, I. R., & Royston, P. (2008). How should variable selection be performed with multiply imputed data? *Statistics in Medicine*, *27*(17), 3227–3246. https://doi.org/10.1002/sim.3177

Woodward, T. S., Moritz, S., Menon, M., & Klinge, R. (2008). Belief inflexibility in schizophrenia. *Cognitive Neuropsychiatry*, *13*(3), 267–277. https://doi.org/10.1080/13546800802099033

Ye, Y., & Lin, L. (2015). Examining Relations between Locus of Control, Loneliness, Subjective Well-Being, and Preference for Online Social Interaction. *Psychological Reports*, *116*(1), 164–175. https://doi.org/10.2466/07.09.PR0.116k14w3

Zammit, S., Odd, D., Horwood, J., Thompson, A., Thomas, K., Menezes, P., Gunnell, D., Hollis, C., Wolke, D., Lewis, G., & Harrison, G. (2009). Investigating whether adverse prenatal and perinatal events are associated with non-clinical psychotic symptoms at age 12 years in the ALSPAC birth cohort. *Psychological Medicine*, *39*(9), 1457–1467. https://doi.org/10.1017/S0033291708005126

Zammit, Stanley, Allebeck, P., Andreasson, S., Lundberg, I., & Lewis, G. (2002). Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: Historical cohort study. *BMJ (Clinical Research Ed.)*, *325*(7374), 1199. https://doi.org/10.1136/bmj.325.7374.1199

Zammit, Stanley, Horwood, J. P., Thompson, A., Birnie, K., Menezes, P., Gunnell, D., Hollis, C., Wolke, D., Lewis, G., & Harrison, G. (2008). Investigating if psychosis-like symptoms (PLIKS) are associated with family history of schizophrenia or paternal age in the ALSPAC birth cohort. *Schizophrenia Research*, *104*(1–3). https://doi.org/10.1016/j.schres.2008.04.036

Zammit, Stanley, Kounali, D., Cannon, M., David, A. S., Gunnell, D., Heron, J., Jones, P. B., Lewis, S., Sullivan, S., Wolke, D., & Lewis, G. (2013). Psychotic experiences and psychotic disorders at age 18 in relation to psychotic experiences at age 12 in a longitudinal population-based cohort study. *The American Journal of Psychiatry*, *170*(7), 742–750. https://doi.org/10.1176/appi.ajp.2013.12060768

Zammit, Stanley, Lewis, G., Rasbash, J., Dalman, C., Gustafsson, J.-E., & Allebeck, P. (2010). Individuals, Schools, and Neighborhood: A Multilevel Longitudinal Study of Variation in Incidence of Psychotic Disorders. *Archives of General Psychiatry*, *67*(9), 914–922. https://doi.org/10.1001/archgenpsychiatry.2010.101

Appendix 1 Abbreviations used in the thesis

Abbreviation	Term
ALSPAC	Avon Longitudinal Study of Parents and Children
BADE	Bias Against Disconfirmatory Evidence
BIC	Bayesian Information Criterion
CAPE	Community Assessment of Psychotic Experiences
CBT	Cognitive Behavoural Therapy
CI	Confidence Interval
CSA	Child Sex Abuse
CSQ	Cognitive Styles Questionnaire
DAG	Directed acyclic graph
DISC	Diagnostic Interview Schedule for Children
DTD	Draws to Decision
ELSPAC	European Longitudinal Study of Pregnancy and Childhood
EMDR	Eye Movement Desensitization and Reprocessing
HMM	Hidden Markov Model
HPA axis	hypothalamic–pituitary–adrenal axis
ICD	International Classification of Diseases
IQ	Intelligence Quotient
IQR	Inter-Quartile Range
JTC Bias	Jumping to Conclusions Bias
LASSO	least absolute shrinkage and selection operator
LOC	Locus of Control
LRS	Likelihood Ratio Statistic
MAR	Missing At Random
MCAR	Missing Completely at Random
MI	Multiple Imputation
MNAR	Missing Not at Random
OR	Odds Ratio
PAF	Population-Attributable Fraction
PDI	Peter's Delusion Inventory
PEs	Psychotic Experiences

PLEs	Psychosis-like Experiences
PLIKSi	Psychosis-Like Symptoms interview
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRS	Polygenic Risk score
PRT	Probabilistic Reasoning Task
PTSD	Post-Traumatic Stress Disorder
RCT	Randomised Control Trial
RR	Relative Risk
RRR	Relative Risk Ratio
SCAN	Schedule for Clinical Assessment in Neuropsychiatry
SMD	Standard Mean Difference
TEA-Ch	Test of Everyday Attention for Childhood
UHR	Ultra-High Risk
WHO	World Mental Health
WISC	Wechsler Intelligence Scale for Children

Appendix 2 Supplementary Information for Methodology Chapter

Appendix Table 2.1 Trauma questions included in trauma measures

Trauma Category	Description	Questionnaire type	Age (years)	Derived Trauma Coding
Bullying	Frequency child has been bullied: 'have you been bullied?'	child-completed	8	TRUE = All the time
Bullying	Frequency child is bullied by sibling	child-completed	12	TRUE = several times a week
Bullying	Bullying OR, Threatened/Blackmailed - Freq	child clinical assessment	8	TRUE = (at least 1/wk& 4+times last 6 months)
Bullying	Bullying OR, Hit/beaten up	child clinical assessment	8	TRUE = (at least 1/wk& 4+times last 6 months)
Bullying	Bullying OR, Threatened/Blackmailed	child clinical assessment	10	TRUE = (at least 1/wk& 4+times last 6 months)
Bullying	Bullying OR, Hit/beaten up	child clinical assessment	10	TRUE = Any positive response
Bullying	Frequency someone threatened/blackmailed teenager	child clinical assessment	12.5	TRUE = Frequently (>4 times) and Very frequently (>1/week)
Bullying	Frequency someone has hit/beaten up teenager	child clinical assessment	12.5	TRUE = Frequently and Very frequently
Bullying	child is Bullied> 6 MTHs	mother based	4	TRUE= Definitely Applies
Bullying	child Been Bullied In Past 6 Mths	child based	7	TRUE = certainly true
Bullying	child is picked on or bullied by other children in past 6 months	child based	9	TRUE = Certainly True
Bullying	Study child has been picked on or bullied by other children in the past six months	mother based	8.1	TRUE = Certainly Applies
Bullying	Child has been picked on or bullied by other children in the last six months	partner based	4	TRUE = certainly applies
Bullying	In past six months, Teenager is often picked on or bullied by other children	child based	13	TRUE = certainly true
Bullying	In the past 6 months, study teenager is picked on or bullied by other teenagers	child based	16	TRUE = certainly true
Emotional Abuse	Partner was emotionally cruel to children since PREG	mother based	18 wks	TRUE = Any positive response
Emotional Abuse	Partner emotionally cruel to children since baby was born	mother based	0.67	TRUE = Any positive response
Emotional Abuse	Mum emotionally cruel to children since baby was born	mother based	0.67	TRUE = Any positive response

Emotional Abuse	Partner emotionally cruel to children >child8MTHs	mother based	2	TRUE = Any positive response
Emotional Abuse	Mum emotionally cruel to children >child8MTHs	mother based	2	TRUE = Any positive response
Emotional Abuse	Partner emotionally cruel to children >child18 mths	mother based	3	TRUE = Any positive response
Emotional Abuse	Mum emotionally cruel to children >child18 mths	mother based	3	TRUE = Any positive response
Emotional Abuse	PTR Emotional Cruel to children> child 30 MTHs y/n	mother based	4	TRUE = Any positive response
Emotional Abuse	MUM Emotional Cruel to children> child 30 MTHs y/n	mother based	4	TRUE = Any positive response
Emotional Abuse	Mothers partner was emotionally cruel to children in past year	mother based	5	TRUE = Any positive response
Emotional Abuse	Mother was emotionally cruel to children in past year	mother based	5	TRUE = Any positive response
Emotional Abuse	Respondent's partner was emotionally cruel to respondent's children since study child's 5th birthday	mother based	6	TRUE = Any positive response
Emotional Abuse	Mother's husband/partner was emotionally cruel to her children since the study child's 6th birthday	mother based	9	TRUE = Any positive response
Emotional Abuse	Mother was emotionally cruel to her children since the study child's 6th birthday	mother based	9	TRUE = Any positive response
Emotional Abuse	PTNR EMOT cruel to child, Y/N since baby was born	partner based	0.16	TRUE = Any positive response
Emotional Abuse	Partner Emotionally Cruel to children since baby was born	partner based	0.67	TRUE = Any positive response
Emotional Abuse	Self Emotionally Cruel to children since baby was born	partner based	0.67	TRUE = Any positive response
Emotional Abuse	Partner Emotionally Cruel To child Y/N since baby was born	partner based	2	TRUE = Any positive response
Emotional Abuse	Self Emotionally Cruel To child Y/N since baby was born	partner based	2	TRUE = Any positive response
Emotional Abuse	Partner's partner was emotionally cruel to their children since study child was 18 months old	partner based	3	TRUE = Any positive response
Emotional Abuse	Partner was emotionally cruel to their children since study child was 18 months old	partner based	3	TRUE = Any positive response
Emotional Abuse	Degree to which emotional cruelty from a partner towards children affected partner since study child was 2.5 years old	partner based	4	TRUE = Any positive response
Emotional Abuse	Degree to which partner's emotional cruelty towards children affected partner since study child was 2.5 years old	partner based	4	TRUE = Any positive response
Emotional Abuse	Respondent's assessment of how much their partner being emotionally cruel to the children in the last year has affected them	partner based	5	TRUE = Any positive response

Emotional Abuse	Respondent's assessment of how much being emotionally cruel to their children in the last year has affected them	partner based	5	TRUE = Any positive response
Emotional Abuse	Respondent's assessment of how much partner's emotional cruelty to children since study child's 5th birthday has affected them	partner based	6	TRUE = Any positive response
Emotional Abuse	Respondent's assessment of how much being emotionally cruel to children since study child's 5th birthday has affected them	partner based	6	TRUE = Any positive response
Emotional Abuse	Father's wife/partner was emotionally cruel to his children since the study child's 6th birthday	partner based	9	TRUE = Any positive response
Emotional Abuse	Father was emotionally cruel to his children since the study child's 6th birthday	partner based	9	TRUE = Any positive response
Emotional Abuse	Respondent's wife/partner has been emotionally cruel to their children since the study child's 9th birthday	partner based	11	TRUE = Any positive response
Emotional Abuse	Respondent has been emotionally cruel to their children since the study child's 9th birthday	partner based	11	TRUE = Any positive response
Emotional Abuse	Respondent's husband/partner has been emotionally cruel to their children since study child's 9th birthday	mother based	11	TRUE = Any positive response
Emotional Abuse	Respondent has been emotionally cruel to their children since study child's 9th birthday	mother based	11	TRUE = Any positive response
Emotional Abuse	Respondent's partner was emotionally cruel to respondent's children in last year	mother based	18	TRUE = Any positive response
Emotional Abuse	Frequency adult in family said hurtful or insulting things to the respondent before 11	child-completed	22	True = Often and Very Often
Emotional Abuse	Frequency adult in family threatened to kick punch, hit respondent with force pre-11	child-completed	22	True = Often and Very Often
Emotional Abuse	Frequency adult outside the family threatened to kick, punch, hit respondent with something that could hurt respondent or physically attacked respondent in another way before age of 11	child-completed	22	TRUE = Sometimes, Often, Very Often
Emotional Abuse	Frequency adult in family said hurtful or insulting things to the respondent 11-17	child-completed	22	TRUE = Sometimes, Often, Very Often

Emotional Abuse	Frequency adult in family pushed, grabbed or shoved respondent between ages of 11 and 17	child-completed	22	TRUE = Sometimes, Often, Very Often
Emotional Abuse	Frequency adult in family threatened to kick punch, hit respondent with force 11-17	child-completed	22	TRUE = Sometimes, Often, Very Often
Emotional Abuse	Frequency adult outside the family threatened to kick, punch, hit respondent with something that could hurt respondent or physically attack respondent in another way between ages of 11 and 17	child-completed	22	TRUE = Sometimes, Often, Very Often
Emotional Neglect	Frequency child feels left out of things	child-completed	8	TRUE = Always
Emotional Neglect	Study child's parent(s) is easy to talk to	child-completed	9.5	TRUE = Not true/mostly untrue
Emotional Neglect	Frequency over last term parents have asked YP about their plans for the future	child-completed	16	TRUE = never
Emotional Neglect	Frequency carers take time to listen, when teenager talks about what happened in their free time	child clinical assessment	12.5	TRUE = never
Emotional Neglect	Frequency carers take time to listen, when teenager talks about what happened in free time	child clinical assessment	13.5	TRUE = never
Emotional Neglect	Frequency parents knew where YP was going, when YP went out, in last year	child clinical assessment	15.5	TRUE = never
Emotional Neglect	Frequency carer listens to YP, when they talk about what they they did in their free time	child clinical assessment	15.5	TRUE = never
Physical Abuse	Partner hurt child since PREG	mother based	gestation	
Physical Abuse	Partner physically cruel to children since baby was born	mother based	0.67	TRUE = Any positive response
Physical Abuse	Mum physically cruel to children since baby was born	mother based	0.67	TRUE = Any positive response
Physical Abuse	Someone they have been out with has intentionally slapped teenager	child clinical assessment	13.5	TRUE = Any positive response
Physical Abuse	Someone they have been out with has intentionally kicked teenager	child clinical assessment	13.5	TRUE = Any positive response
Physical Abuse	Someone they have been out with has intentionally bent fingers of teenager	child clinical assessment	13.5	TRUE = Any positive response
Physical Abuse	Someone they have been out with has intentionally hit with their fist teenager	child clinical assessment	13.5	TRUE = Any positive response
Physical Abuse	Partner physically cruel to children >child8MTHs	mother based	2	TRUE = Any positive response

Physical Abuse	Mum physically cruel to children >child8MTHs	mother based	2	TRUE = Any positive response
Physical Abuse	Partner physically cruel to children>child18 mths	mother based	3	TRUE = Any positive response
Physical Abuse	Mum physically cruel to children >child18 mths	mother based	3	TRUE = Any positive response
Physical Abuse	Partner physically Cruel to children> child 30 MTHs y/n	mother based	4	TRUE = Any positive response
Physical Abuse	MUM physically Cruel to children> child 30 MTHs y/n	mother based	4	TRUE = Any positive response
Physical Abuse	Mothers partner was physically cruel to children in past year	mother based	5	TRUE = Any positive response
Physical Abuse	Mother was physically cruel to children in past year	mother based	5	TRUE = Any positive response
Physical Abuse	Frequency that child is slapped or hit by mother (this q is asked about girls only)	child based/reported by mother	12	TRUE = once/twice a week, several times a week, daily
Physical Abuse	Respondent's partner physically cruel to respondent's children since study child's 5th birthday	mother based	6	TRUE = Any positive response
Physical Abuse	Respondent physically cruel to own children since study child's 5th birthday	mother based	6	TRUE = Any positive response
Physical Abuse	Mother's husband/partner was physically cruel to her children since the study child's 6th birthday	mother based	9	TRUE = Any positive response
Physical Abuse	Mother was physically cruel to her children since the study child's 6th birthday	mother based	9	TRUE = Any positive response
Physical Abuse	PTNR hurt child since PTNR PREG, Y/N	partner based	gestation	
Physical Abuse	Partner Physically Cruel to children	partner based	0.67	TRUE = Any positive response
Physical Abuse	Self Physically Cruel to children	partner based	0.67	TRUE = Any positive response
Physical Abuse	Partner Physically Cruel to child Y/N	partner based	2	TRUE = Any positive response
Physical Abuse	Self Physically Cruel to child Y/N	partner based	2	TRUE = Any positive response
Physical Abuse	Partner's partner was physically cruel to their children since study child was 18 months old	partner based	3	TRUE = Any positive response
Physical Abuse	Partner was physically cruel to their children since study child was 18 months old	partner based	3	TRUE = Any positive response
Physical Abuse	Degree to which physical cruelty from a partner to children affected partner since study child was 2.5 years old	partner based	4	TRUE = Any positive response
Physical Abuse	Degree to which partner being physically cruel to children affected partner since study child was 2.5 years old	partner based	4	TRUE = Any positive response

Physical Abuse	Respondent's assessment how much their partner being physically cruel to the children in the last year has affected them	partner based	5	TRUE = Any positive response
Physical Abuse	Respondent's assessment of how much being physically cruel to the children in the last year has affected them	partner based	5	TRUE = Any positive response
Physical Abuse	Respondent's assessment of how much partner's physical cruelty to children since study child's 5th birthday has affected them	partner based	6	TRUE = Any positive response
Physical Abuse	Respondent's assessment of how much being physically cruel to children since study child's 5th birthday has affected them	partner based	6	TRUE = Any positive response
Physical Abuse	Father's wife/partner was physically cruel to his children since the study child's 6th birthday	partner based	9	TRUE = Any positive response
Physical Abuse	Father was physically cruel to his children since the study child's 6th birthday	partner based	9	TRUE = Any positive response
Physical Abuse	Respondent's wife/partner was physically cruel to their children since the study child's 9th birthday	partner based	11	TRUE = Any positive response
Physical Abuse	Respondent was physically cruel to their children since the study child's 9th birthday	partner based	11	TRUE = Any positive response
Physical Abuse	Respondent's husband/partner was physically cruel to their children since study child's 9th birthday	mother based	11	TRUE = Any positive response
Physical Abuse	Respondent was physically cruel to their children since the study child's 9th birthday	mother based	11	TRUE = Any positive response
Physical Abuse	Respondent's partner was physically cruel to respondent's children in last year	mother based	18	
Physical Abuse	Respondent was physically cruel to own children in last year	mother based	18	
Physical Abuse	When teenager has rages or tantrums how often does parent: slap or hits study teenager	child based	16	TRUE = always
Physical Abuse	Frequency that respondent hits or slaps study teenager	child based	16	TRUE = At least once a week
Physical Abuse	Frequency YP's partners have used physical force such as pushing, slapping, hitting or holding them down	child-completed	22	True = Any Positive Response

Physical Abuse	Frequency YP's partners have used more severe physical force such as punch, strangling, beating them up, hitting them with an object	child-completed	22	True = Any Positive Response
Physical Abuse	Frequency adult in family pushed, grabbed or shoved respondent	child-completed	22	True = Often and Very Often
Physical Abuse	Frequency adult in family punished respondent in a way that seemed cruel	child-completed	22	True = Often and Very Often
Physical Abuse	Frequency adult in family actually kicked, punched, hit respondent with some force	child-completed	22	True = Any Positive Response
Physical Abuse	Frequency adult in family hit respondant so hard it left marks	child-completed	22	True = Any Positive Response
Physical Abuse	Frequency adult outside the family actually kicked punched, hit respondent with something that could hurt respondent or physically attacked respondent in another way before age of 11	child-completed	22	True = Any Positive Response
Sexual Abuse	child sexually abused since 6 months old (adj)	child based	1.5	TRUE = Any positive response
Sexual Abuse	child sexually abused > 18 months, Y/N	child based	2.5	TRUE = Any positive response
Sexual Abuse	child Sexually Abused Y/N	child based	3.5	TRUE = Any positive response
Sexual Abuse	D6: child was sexually abused since age 3	child based	5	TRUE = Any positive response
Sexual Abuse	D6: child sexually abused in past 15 months	child based	6	TRUE = Any positive response
Sexual Abuse	DV: child was sexually abused since his/her 5th birthday (Y/N)	child based	7	TRUE = Any positive response
Sexual Abuse	E6: Since 7th birthday child has been sexually abused	child based	9	TRUE = Any positive response
Sexual Abuse	YPA5008: e1e: Frequency YP's partners have pressured them into kissing/touching/something else (under/over 18)	child-completed	22	TRUE = Any positive response
Sexual Abuse	YPA5010: e1f: Frequency YP's partners have physically forced them into kissing/touching/something else (under/over 18)	child-completed	22	TRUE = Any positive response
Sexual Abuse	Frequency YP's partners have pressured them into having sexual intercourse (under/over 18)	child-completed	22	TRUE = Any positive response
Sexual Abuse	Frequency YP's partners have physically forced them into having sexual intercourse (under/over 18)	child-completed	22	TRUE = Any positive response

Sexual Abuse	11-17, were you touched in a sexual way by an adult or an older child or were you forced to touch an adult or older child in a sexual way when you did not want to?	child-completed	22	TRUE = Any positive response
Sexual Abuse	11-17 Adult or older child forced, or attempted to force, child into sexual activity	child-completed	22	TRUE = Any positive response
Sexual Abuse	Respondent was touched in a sexual way by adult or older child, or was forced to touched adult or older child in a sexual way, before age of 11	child-completed	22	TRUE = Any positive response
Sexual Abuse	pre-11 Adult or older child forced, or attempted to force, child into sexual activity	child-completed	22	TRUE = Any positive response
Domestic Violence	PTNR hurt MUM since MID PREG	mother based	0.16	TRUE = Any positive response
Domestic Violence	Physically hurt by partner since baby was born	mother based	0.67	TRUE = Any positive response
Domestic Violence	PTNR emotionally cruel to MUM >child born born	mother based	0.67	TRUE = Any positive response
Domestic Violence	Partner physically cruel to Mum >child8MTHs	mother based	2	TRUE = Any positive response
Domestic Violence	Partner physically cruel to mother >child18 mths	mother based	3	TRUE = Any positive response
Domestic Violence	Partner physically Cruel to MUM> child 30 MTHs y/n	mother based	4	TRUE = Any positive response
Domestic Violence	Mothers partner was physically cruel to her in past year	mother based	5	TRUE = Any positive response
Domestic Violence	Respondent's partner was physically cruel to them since study child's 5th birthday	mother based	6	TRUE = Any positive response
Domestic Violence	Mother has ever thrown an object at partner	mother based	8	TRUE = Often
Domestic Violence	Partner has ever thrown an object at mother	mother based	8	TRUE = Often
Domestic Violence	Mother has ever kicked, bitten or hit partner with a fist	mother based	8	TRUE = Often
Domestic Violence	Partner has ever kicked, bitten or hit mother with a fist	mother based	8	TRUE = Often
Domestic Violence	Mother has ever tried to hit partner with something	mother based	8	TRUE = Often
Domestic Violence	Partner has ever tried to hit mother with something	mother based	8	TRUE = Often
Domestic Violence	Mother has ever physically twisted partner's arm	mother based	8	TRUE = Often
Domestic Violence	Partner has ever physically twisted mother's arm	mother based	8	TRUE = Often
Domestic Violence	Mother has ever tried to throw partner bodily	mother based	8	TRUE = Often
Domestic Violence	Partner has ever tried to throw mother bodily	mother based	8	TRUE = Often
Domestic Violence	Mother has ever beaten partner up	mother based	8	TRUE = Often & Sometimes
Domestic Violence	Partner has ever beaten mother up	mother based	8	TRUE = Often & Sometimes

Domestic Violence	Mother has ever tried to choke or strangle partner	mother based	8	TRUE = Often & Sometimes
Domestic Violence	Partner has ever tried to choke or strangle mother	mother based	8	TRUE = Often & Sometimes
Domestic Violence	Mother has ever threatened partner with a knife or other weapon	mother based	8	TRUE = Often & Sometimes
Domestic Violence	Partner has ever threatened mother with a knife or other weapon	mother based	8	TRUE = Often & Sometimes
Domestic Violence	Mother has ever used a knife or other weapon on partner	mother based	8	TRUE = Often & Sometimes
Domestic Violence	Partner has ever used a knife or other weapon on mother	mother based	8	TRUE = Often & Sometimes
Domestic Violence	Mother's husband/partner was physically cruel to her since the study child's 6th birthday	mother based	9	TRUE = Any positive response
Domestic Violence	PTNR phys. hurt you since MID PREG, Y/N	partner based	0.16	TRUE = Any positive response
Domestic Violence	Partner Physically Cruel Since Baby was Born	partner based	0.67	TRUE = Any positive response
Domestic Violence	Partner Physically Cruel Y/N since baby was 8 months old	partner based	2	True = Any Positive Response
Domestic Violence	Partner's partner was physically cruel to them since study child was 18 months old	partner based	3	TRUE = Any positive response
Domestic Violence	Degree to which physical cruelty from a partner affected partner since child was 2.5 years old	partner based	4	TRUE = Any positive response
Domestic Violence	Respondent's assessment of how much their partner being physically cruel in the last year has affected them	partner based	5	TRUE = Any positive response
Domestic Violence	Respondent's assessment of how much partner being physically cruel since study child's 5th birthday has affected them	partner based	6	TRUE = Any positive response
Domestic Violence	Respondent has thrown an object at their partner which could have hurt them	partner based	8	TRUE = Often
Domestic Violence	Respondent's partner has thrown an object at them which could have hurt them	partner based	8	TRUE = Often
Domestic Violence	Respondent has ever bitten/kicked/hit their partner with a fist	partner based	8	TRUE = Often
Domestic Violence	Respondent's partner has ever bitten/kicked/hit them with a fist	partner based	8	TRUE = Often
Domestic Violence	Respondent has tried to hit their partner with something	partner based	8	TRUE = Often
Domestic Violence	Respondent's partner has tried to hit them with something	partner based	8	TRUE = Often
Domestic Violence	Respondent has tried to twist their partner's arm	partner based	8	TRUE = Often

Domestic Violence	Respondent's partner has tried to twist their arm	partner based	8	TRUE = Often
Domestic Violence	Respondent has ever thrown/tried to throw their partner	partner based	8	TRUE = Often
Domestic Violence	Respondent's partner has ever thrown/tried to throw them	partner based	8	TRUE = Often
Domestic Violence	Respondent has ever beaten up their partner	partner based	8	TRUE = Often & Sometimes
Domestic Violence	Respondent's partner has ever beaten them up	partner based	8	TRUE = Often & Sometimes
Domestic Violence	Respondent has ever tried to choke their partner	partner based	8	TRUE = Often & Sometimes
Domestic Violence	Respondent's partner has ever tried to choke them	partner based	8	TRUE = Often & Sometimes
Domestic Violence	Respondent has ever threatened their partner with a knife/weapon	partner based	8	TRUE = Often & Sometimes
Domestic Violence	Respondent's partner has ever threatened them with a knife/weapon	partner based	8	TRUE = Often & Sometimes
Domestic Violence	Respondent has ever used a knife/weapon on their partner	partner based	8	TRUE = Often & Sometimes
Domestic Violence	Respondent's partner has ever used a knife/weapon on them	partner based	8	TRUE = Often & Sometimes
Domestic Violence	Father's wife/partner was physically cruel to him since the study child's 6th birthday	partner based	9	TRUE = Any positive response
Domestic Violence	Father/wife/partner threw or broke things in the past 3 months	partner based	9	TRUE = Any positive response
Domestic Violence	Respondent's wife/partner was physically cruel to them since the study child's 9th birthday	partner based	11	TRUE = Any positive response
Domestic Violence	Partner and partner's partner hit or slapped each other in the past 3 months	partner based	12	TRUE = Any positive response
Domestic Violence	Respondent's husband/partner was physically cruel to them since study child's 9th birthday	mother based	11	TRUE = Any positive response
Domestic Violence	Mother or partner have hit or slapped each other in the past 3 months	mother based	12	TRUE = Any positive response
Domestic Violence	Respondent's partner was physically cruel to respondent in last year	mother based	18	TRUE = Any positive response

Appendix Table 2.2 Coding procedure for Trauma Variables complete-case trauma variables according to missing data

Trauma Type	Code	Criterion
Trauma type at each period	1	A yes to any of the questions asked with the remainder being missing and/or no.
	0	No positive responses combined with negative responses to at least 50% of questionnaires with the remainder being missing
	Missing	No positive responses combined with up to negative responses on 4 or less of the 10 questionnaires with the remainder being missing
Any Reported Trauma at each age-period	1	A yes to any of the 5 individual trauma type categories during the age-period asked with the remainder being yes or no.
	0	No positive responses combined with negative responses to all 5 trauma categories during the age-period
	Missing	No positive responses combined with no response to one of the trauma categories during the age-period
Any Reported Trauma 0-17 years	1	A yes to trauma during any of the 3 age-periods categories with the remainder being yes or no.
	0	No positive responses combined with negative responses the 3 trauma timing categories with the remainder being yes or no.
	Missing	No positive responses combined with no response to one of the 3 trauma timing categories

Appendix 3 Supplementary Information for Study I

Appendix Table 3.1 Correlation between trauma variables

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)	(20)
(1) Physical Abuse 0-5	1.00																			
(2) Emotional Abuse 0-5	0.72	1.00																		
(3) Bullying 0-5	0.07	0.02	1.00																	
(4) Sexual Abuse 0-5	-	-	-	-	-															
(5) Domestic Violence 0-5	0.50	0.57	0.02	0.17	1.00															
(6) Any Reported Trauma 0-5	1.00	1.00	1.00	1.00	1.00	1.00														
(7) Physical Abuse 5-11	0.47	0.30	0.04	0.36	0.37	0.36	1.00													
(8) Emotional Abuse 5-11	0.56	0.57	0.02	0.14	0.41	0.52	0.61	1.00												
(9) Emotional Neglect 5-11	0.14	0.07	0.21	1.00	0.06	0.10	0.15	0.11	1.00											
(10) Bullying 5-11	0.11	0.07	0.03	1.00	0.01	0.06	0.22	0.13	0.31	1.00										
(11) Sexual Abuse 5-11	0.18	0.24	0.04	1.00	0.04	0.16	0.16	0.23	0.26	0.16	1.00									
(12) Domestic Violence 5-11	0.39	0.33	0.05	0.19	0.57	0.48	0.39	0.47	0.13	0.10	0.01	1.00								
(13) Any reported Trauma 5-11	0.45	0.36	0.01	0.08	0.39	0.39	1.00	1.00	1.00	1.00	1.00	1.00	1.00							
(14) Physical Abuse 11-17	0.15	0.16	0.04	0.30	0.20	0.22	0.61	0.35	0.24	0.22	0.23	0.19	0.41	1.00						
(15) Emotional Abuse 11-17	0.36	0.33	0.04	0.23	0.26	0.31	0.59	0.61	0.18	0.16	0.25	0.32	0.47	0.59	1.00					
(16) Bullying 11-17	0.17	0.07	0.05	1.00	0.04	0.07	0.20	0.17	0.18	0.26	0.23	0.07	0.23	0.21	0.23	1.00				
(17) Emotional Neglect 11-17	0.05	0.05	0.02	1.00	0.07	0.06	0.04	0.14	0.30	0.07	0.10	0.09	0.10	0.02	0.16	0.24	1.00			
(18) Sexual Abuse 11-17	0.06	0.08	0.04	0.19	0.03	0.04	0.24	0.19	0.18	0.10	0.45	0.01	0.21	0.56	0.32	0.14	0.13	1.00		
(19) Domestic Violence 11-17	0.22	0.17	0.14	-	0.34	0.30	0.27	0.35	0.16	0.04	0.15	0.57	0.32	0.30	0.58	0.12	0.03	0.07	1.00	
(20) Any reported trauma 11-17	0.22	0.17	0.07	0.10	0.20	0.19	0.48	0.35	0.24	0.23	0.31	0.23	0.38	1.00	1.00	1.00	1.00	1.00	1.00	1.00

Appendix Table 3.2 Associations between exposure to trauma and psychotic experiences at 18 years according to timing and type[1]

		Unadjusted			Adjusted[2]			Adjusted[2,3]		
	% exposed	OR	95% CI	*p*	OR	95% CI	*p*	OR	95% CI	*p*
Trauma Types (0-4.9 years)										
Physical Abuse	4.7	1.32	0.83, 2.09	0.244	1.30	0.82, 2.08	.264	.93	0.56, 1.55	0.781
Emotional Abuse	11.2	1.64	1.21, 2.23	0.002	1.52	1.11, 2.07	.009	1.31	0.83, 1.86	0.125
Bullying	1.7	1.81	0.90, 3.66	0.095	1.71	0.84, 3.48	.137	1.68	0.82, 3.43	0.158
Sexual abuse	0.2	3.52	0.69, 17.85	0.129	2.42	0.46, 12.84	.299	2.47	0.46, 13.26	0.292
Domestic Violence	13.2	2.08	1.60, 2.71	<.001	1.83	1.39, 2.40	<.001	1.71	1.27, 2.29	<.001
Emotional Neglect	-	-	-	-	-	-	-	-	-	-
Trauma Types (5-10.9 years)										
Physical Abuse	10.3	2.07	1.52, 2.84	<.001	1.98	1.45, 2.72	<.001	1.58	1.10, 2.26	0.013
Emotional Abuse	12.9	1.86	1.41, 2.45	<.001	1.77	1.34, 2.35	<.001	1.37	0.98, 1.91	0.062
Bullying	21.6	1.89	1.46, 2.37	<.001	1.91	1.48, 2.44	<.001	1.74	1.34, 2.25	<.001
Sexual abuse	2.8	1.87	1.07, 3.28	0.028	1.50	0.84, 2.67	0.172	1.18	0.64, 2.17	0.589
Domestic Violence	13.1	1.99	1.46, 2.72	<.001	1.75	1.26, 2.43	.001	1.47	1.04, 2.08	0.029
Emotional Neglect	3.5	2.45	1.58, 3.18	<.001	2.32	1.49, 3.63	<.001	1.95	1.23, 3.09	0.004
Trauma Types (11-17 years)										
Physical Abuse	15.6	2.63	2.02, 3.42	<.001	2.43	1.86, 3.18	<.001	1.83	1.36, 2.47	<.001
Emotional Abuse	7.3	2.42	1.75, 3.35	<.001	2.23	1.60, 3.10	<.001	1.40	0.95, 2.06	0.094
Bullying	14.4	2.17	1.69, 2.78	<.001	2.10	1.64, 2.70	<.001	1.87	1.45, 2.42	<.001
Sexual abuse	9.4	3.21	2.31, 4.46	<.001	3.00	2.12, 4.21	<.001	2.34	1.62, 3.37	<.001
Domestic Violence	5.0	1.99	1.22, 3.23	0.006	1.70	1.03, 2.81	.036	1.37	0.80, 2.33	0.246
Emotional Neglect	3.5	2.33	1.56, 3.74	<.001	2.29	1.52, 3.44	<.001	1.96	1.28, 3.00	0.002

Appendix Table 3.2 Note: [1]Imputed dataset, n=4,433 Abbreviation: OR, odds ratio [2]Adjusted for confounders: sex, parental income, parental drug use, maternal education, crowded living conditions [3]Adjusted for other trauma exposures

Appendix Table 3.3 Associations Between Exposure to Trauma and Psychotic Experiences at 18 years According to Timing and Type using complete-case data[a]

	N	Unadjusted			Adjusted[1]			Adjusted[1,2]		
		OR	**95% CI**	***p***	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
Any trauma (0-17 years)	3,710	2.30	1.77, 2.99	<.001	2.20	1.69, 2.86				
Any Trauma (0-4.9 years)	3,411	1.62	1.23, 2.11	.001	1.48	1.13, 1.96	.005			
Any Trauma (5-10.9 years)	2,929	2.03	1.54, 2.66	<.001	2.00	1.52, 2.62	<.001			
Any Trauma (11-17 years)	2,064	2.96	2.11, 4.14	<.001	2.84	2.03, 3.99	<.001			
Physical Abuse	3,588	2.01	1.56, 2.59	<.001	1.98	1.54, 2.56	<.001	1.54	1.12, 2.04	.003
Emotional Abuse		1.67	1.29, 2.16	<.001	1.60	1.24, 2.08	<.001	1.15	.86, 1.55	.340
Bullying		2.08	1.65, 2.63	<.001	2.03	1.61, 2.57	<.001	1.84	1.45, 2.34	<.001
Sexual abuse		1.99	1.41, 2.81	<.001	1.94	1.37, 2.74	<.001	1.53	1.06, 2.21	.022
Domestic Violence		1.71	1.31, 2.23	<.001	1.56	1.19, 2.05	.001	1.32	.99, 1.77	.061
Emotional Neglect		2.18	1.52, 3.11	<.001	2.10	1.47, 3.01	<.001	1.75	1.21, 2.53	.003
Trauma Types (0-4.9 years)	3,411									
Physical Abuse		1.13	.66, 1.96	.649	1.14	.66, 1.99	.625	.88	.481, 1.59	.665
Emotional Abuse		1.38	.972, 1.97	.071	1.30	.91, 1.85	.155	1.15	.77, 1.71	.505
Bullying		2.06	.96, 4.44	.064	2.19	1.01, 4.73	.046	2.15	.99, 4.66	.052
Sexual Abuse		-	-	-	-	-	-	-	-	-
Domestic Violence		1.83	1.33, 2.52	<.001	1.64	1.18, 2.27	.003	1.59	1.13, 2.26	.009
Emotional		-	-	-	-	-	--	-	-	-

Neglect										
Trauma Types (5-10.9 years)	2,929									
Physical Abuse		1.95	1.34, 2.84	<.001	1.92	1.32, 2.80	.001	1.55	1.02, 2.35	.042
Emotional Abuse		1.62	1.12, 2.33	.010	1.58	1.09, 2.28	.015	1.16	0.77, 1.77	.476
Bullying		1.94	1.45, 2.60	<.001	1.99	1.48, 2.67	<.001	1.80	1.33, 2.44	<.001
Sexual Abuse		1.60	.76, 3.40	.217	1.43	.67, 3.07	.355	1.11	.40, 2.44	.804
Domestic Violence		1.88	1.30, 2.70	.001	1.74	1.20, 2.52	.004	1.44	.97, 2.14	.071
Emotional Neglect		2.27	1.29, 4.01	.005	2.24	1.27, 3.98	.006	1.79	.99, 3.23	.055
Trauma Types (11-17 years)	2,064									
Physical Abuse		2.47	1.71, 3.56	<.001	2.38	1.64, 3.46	<.001	1.73	1.23, 2.66	.012
Emotional Abuse		2.61	1.62, 4.15	<.001	2.51	1.57, 4.01	<.001	1.61	.94, 2.75	.082
Bullying		3.20	2.22, 4.61	<.001	3.07	2.12, 4.44	<.001	2.77	1.90, 4.04	<.001
Sexual Abuse		2.53	1.64, 3.91	<.001	2.46	1.58, 3.85	<.001	1.75	1.08, 2.85	.024
Domestic Violence		1.57	.77, 3.21	.213	1.43	.69, 2.94	.336	1.04	.48, 2.27	.918
Emotional Neglect		2.48	1.34, 4.60	.004	2.43	1.30, 4.54	.005	1.91	.99, 3.68	.053

Abbreviation: OR, odds ratio [a]Adjusted for confounders: sex, parental income, parental drug use, maternal education, crowded living conditions [b]Adjusted for other trauma exposures

Appendix Table 3.4 Associations Between Exposure to Trauma and Psychotic Experiences at 18 Years According to Number of Trauma Types at Each Age-Period using complete-case data

Time Point			**Unadjusted**			**Adjusted[a]**		
	N	**Trauma Frequency n(%)**	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
0-4.9 years	3,758	1 – 513 (13.7)	1.64	1.21, 2.20	.001	1.50	1.11, 2.04	.008
		2 – 190 (5.1)	1.82	1.17, 2.83	.008	1.66	1.06, 2.59	.027
		3+ - 53 (1.41)	1.54	.65, 3.63	.328	1.51	.64, 3.59	.350
		Linear trend	1.33	1.14, 1.56	<.001	1.28	1.09, 1.50	.002
5 – 10.9 years		1 – 972 (26.0)	1.57	1.21, 2.04	.001	1.57	1.20, 2.04	.001
		2 – 323 (8.6)	2.00	1.39, 2.88	<.001	1.96	1.35, 2.83	<.001
		3+ - 129 (3.4)	3.14	1.96, 5.04	<.001	3.07	1.90, 4.95	<.001
		Linear trend	1.45	1.28, 1.65	<.001	1.44	1.27, 1.64	<.001
11 – 16.9 years		1 -847 (22.5)	1.70	1.30, 2.22	<.001	1.67	1.27, 2.19	<.001
		2 – 249 (6.6)	3.06	2.13, 4.40	<.001	2.94	2.04, 4.233	<.001
		3+ - 50 (1.33)	8.03	4.42, 14.6	<.001	6.94	3.78, 12.73	<.001
		Linear trend	1.83	1.60, 2.10	<.001	1.78	1.55, 2.04	<.001

Abbreviation: OR, odds ratio [a]Adjusted for confounders: sex, parental income, parental drug use, maternal education, crowded living conditions

Appendix Table 3.5 Associations Between Number of Timepoints Trauma is Reported and Psychotic Experiences at 18 Years using complete-case data

		Unadjusted			**Adjusted[b]**		
N	**Trauma Frequency n(%)**	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
3,758[a]	1 – 1,182 (31.4)	1.48	1.13, 1.94	.004	1.48	1.13, 1.94	.004
	2 – 538 (14.3)	2.27	1.67, 3.08	<.001	2.23	1.64, 3.04	<.001
	3 – 107 (2.85)	2.34	1.33, 4.19	.003	2.45	1.37, 4.38	.002
	Linear Trend	1.44	1.26, 1.63	<.001	1.43	1.26, 1.64	<.001

Abbreviation: OR, odds ratio [a]Number of timepoints (early childhood/mid-childhood/adolescence) Trauma exposure is reported [b]Adjusted for confounders: sex, parental income, parental drug use, maternal education, crowded living

Appendix Table 3.6 Associations Between Trauma Reported by Child or Parent[a] and psychotic experiences reported at 18 years of age exposures using complete-case data

			Unadjusted			Adjusted[b]		
Age-period		**N**	**OR**	**95% CI**	***p***	**OR**	**95% CI**	***p***
5-10.9 years	Parent-reported	3,615	1.64	1.23, 2.19	.001	1.63	1.22, 2.18	.001
	Child-reported		1.86	1.45, 2.38	<.001	1.86	1.44, 2.39	<.001
11-17 years	Parent-reported	3,512	2.21	1.53, 3.19	<.001	2.18	1.50, 3.18	<.001
	Child-reported		2.24	1.74, 2.87	<.001	2.16	1.68, 2.78	<.001

Abbreviation: OR, odds ratio [a]The following categories included were derived using a number retrospective questionnaires at 22 years of age and data from these questions are omitted in this analysis: 5-10.9 years: physical abuse, emotional abuse, sexual abuse, 11-17 years: physical abuse, emotional abuse, sexual abuse [b]Adjusted for confounders: sex, parental income, parental drug use, maternal education, crowded living conditions

Appendix 4 Supplementary Information for Study II

Figure 4.1 Search Protocol

Psychinfo search 17/10/17

1. (JTC or (Jumping adj2 conclusions) or (jump adj2 conclusion) or (data adj gathering) or (beads adj2 task) or probab* reas*).ti,ab,id,tm.
2. (bias adj2 (cognition or cognitive or attention* or process* or perception or perceptual or cognition)).ti,ab,id,tm.
3. (trauma* or maltreat* or abuse or advers* or neglect or bully* or victim* or rape or violen* or assault*).ti,ab,id,tm.
4. ((source adj memory) or (source adj monitoring) or (reality adj monitoring) or (reality adj discrimination) or (source adj recognition) or (external adj monitoring) or (external adj misattribut*) or (internal adj attribut*)).ti,ab,id,tm.
5. "locus of control".ti,ab,id,tm.
6. ((attribut* adj style) or (external adj attribut*) or (attribut* adj style) or (externalis* adj bias) or (externaliz* adj bias)).ti,ab,id,tm.
7. (belief inflex* or BADE or bias against disconfirmatory evidence or disconfirm* bias* or evidence integrat*).ti,ab,id,tm.
8. ((Top-down adj2 process*) or (top adj down adj2 process*) or (auditory adj feedback) or (visual adj feedback)).ti,ab,id,tm.
9. 1 and 3
10. 2 and 3
11. 3 and 4
12. 3 and 5
13. 3 and 6
14. 3 and 7
15. 3 and 8

OVID Medline® **search 1946 to 17/10/17**

1. (trauma* or maltreat* or abuse or advers* or neglect or bully* or victim* or rape or violen* or assault*).ti,ab,kf.
2. (bias adj2 (cognition or cognitive or attention* or process* or perception or perceptual or cognition)).ti,ab,kf.
3. (JTC or (Jumping adj2 conclusions) or (jump adj2 conclusion) or (data adj gathering) or (beads adj2 task) or probab* reas*).ti,ab,kf.
4. ((source adj memory) or (source adj monitoring) or (reality adj monitoring) or (reality adj discrimination) or (source adj recognition) or (external adj monitoring) or (external adj misattribut*) or (internal adj attribut*)).ti,ab,kf.
5. "locus of control".ti,ab,kf.
6. ((external adj attribut*) or (attribut* adj style) or (externalis* adj bias) or (externaliz* adj bias)).ti,ab,kf.
7. ((Top-down adj2 process*) or (top adj down adj2 process*) or (auditory adj feedback) or (visual adj feedback)).ti,ab,kf.

8. 1 and 2

9. 1 and 3

10. 1 and 4

11. 1 and 5

12. 1 and 6

13. 1 and 7

PILOTS search 18/10/17

(((Top-down NEAR/2 process*) OR (top down NEAR/2 process*) OR (auditory NEAR/1 feedback) OR (visual NEAR/1 feedback)) AND (trauma* OR maltreat* OR abuse OR advers* OR neglect OR bully* OR victim* OR rape OR violen* OR assault*)) AND stype.exact("Scholarly Journals")

((belief NEAR/1 inflex*) OR BADE OR (bias NEAR/1 against NEAR/1 disconfirmatory NEAR/1 evidence) OR (disconfirm* NEAR/1 bias*) OR (evidence NEAR/1 integrat*)) AND (trauma* OR maltreat* OR abuse OR advers* OR neglect OR bully* OR victim* OR rape OR violen* OR assault*) AND stype.exact("Scholarly Journals")

("locus of control" OR ((attribut* NEAR/1 style) OR (external NEAR/1 attribut*) OR (attribut* NEAR/1 style) OR (externalis* NEAR/1 bias) OR (externaliz* NEAR/1 bias))) AND (trauma* OR maltreat* OR abuse OR advers* OR neglect OR bully

* OR victim

* OR rape OR violen* OR assault*)

Figure 4.2 Screening Checklist

((source NEAR/1 memory) OR (source NEAR/1 monitoring) OR (reality NEAR/1 monitoring) OR (reality NEAR/1

Is the paper published in a peer-reviewed journal? Y/N
Does the paper include a measure of trauma or childhood adversity? Y/N
Trauma/adversity should refer to:

- Physical abuse
- Emotional abuse
- Sexual Abuse
- Neglect
- Bullying

And any exposures where the person was exposed to: death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence.

Stressful life events such as parental divorce / economic adversity, and other events that do not fit in criteria above are not to be included

Trauma reports must include measures of trauma that have occurred prior to the age of 18 years old Y/N
Does the study measure a cognitive bias listed in the protocol **or** specifically state that it measures a cognitive bias associated with psychosis? Y/N
Does the study compare groups of participants who do and do not report childhood trauma/adversity on a cognitive bias task Y/N

discrimination) OR (source NEAR/1 recognition) OR (external NEAR/1 monitoring) OR (external NEAR/1 misattribut*) OR (internal NEAR/1 attribut*)) AND (trauma* OR maltreat* OR abuse OR advers* OR neglect OR bully* OR victim* OR rape OR violen* OR assault*) AND stype.exact("Scholarly Journals")

((JTC) OR (Jumping NEAR/2 conclusions) OR (jump NEAR/2 conclusion) OR (data NEAR/2 gathering) OR (beads NEAR/2 task) OR (probab* reas*)) AND (trauma* OR maltreat* OR abuse OR advers* OR neglect OR bully* OR victim* OR rape OR violen* OR assault*) AND stype.exact("Scholarly Journals")

Figure 4.3 Adapted Newcastle-Ottawa Quality Assessment

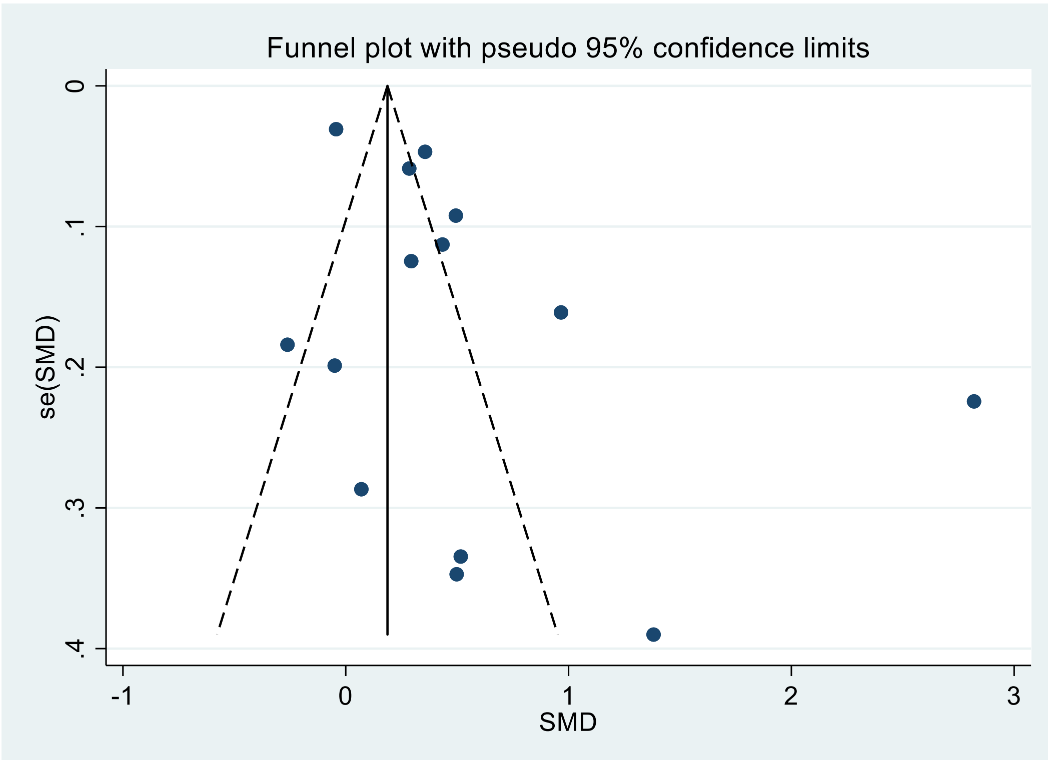
1) Selection of Participants
   a) Reported as randomly or consecutively (completely) sampled*
   b) Reported as sampled using convenience sampling
   c) No description or unclear description of recruitment method
2) Selection of the non-exposed cohort
   a) Drawn from the same community and representative of the exposed cohort*
   b) Drawn from a different source
   c) No description of the derivation of the non-exposed cohort
3) Selection of recruited participants
   a) Response rate of over 75% from selected participant reported*
   b) No reported response rate
4) Comparability
   a) The study controls for two of the following factors: sex, SES, IQ, family history of psychopathology **
   b) The study controls for one of the factors above*
   c) No adjustment for any of the confounders listed above
5) Assessment of outcome
   a) Independent assessment blind to trauma status *
   b) Self-report*
   c) No description/ other

Note * denotes one point on the quality assessment scale and fulfils the quality assessment criteria

Appendix Table 4.1 Methods of Trauma Assessment in Studies Included in the Review

Study	Trauma Type	Trauma Measure	Scale
Allen et al., 2017	Multiple	Questionnaire	Questions in PTSD section of adult co-morbidity survey
Andreou, 2000	Bullying	Questionnaire	Bullying-Behaviour Scale and the Peer-Victimisation Scale(Austin & Joseph, 1996)
Asberg & Renk, 2014	Sexual Abuse	Questionnaire	Life events checklist
Atik & Guneri, 2013	Bullying	Questionnaire	Revised Olweus Bully/Victim Questionnaire (OBVQ) (Gonçalves et al., 2016)
Barahal, Waterman, & Martin, 1981	Multiple	Referrals from social services	N/A
Beck -Sander 1997	Sexual & Physical Abuse	Questionnaire	Sex Events Questionnaire (adapted) (Calam & Slade, 1989) and Physical abuse record (Andrews & Brown, 1988)
Bendall 2011	Multiple	Questionnaire	Childhood Trauma Questionnaire (Bernstein et al., 1997)
Bolstad 1997	Sexual Abuse	Questionnaire	Self-report measure developed by study authors
Chiu et al., 2016	Multiple	Questionnaire	The Brief Betrayal Trauma Survey (Goldberg & Freyd, 2006)
Fredstrom, Adams, & Gilman, 2011	Bullying	Questionnaire	Self-report measure developed by study authors
Freeman, Pugh, & Garety, 2008	Multiple	Questionnaire	Life stressor checklist - child trauma section(Wolfe, J., Kimerling, R., 1997)
Hovens, Giltay, van Hemert, & Penninx, 2016	Multiple	Questionnaire	NEMESIS childhood trauma interview(J. G. F. M. Hovens et al., 2012)
Ireland, Alderson, & Ireland, 2015	Sexual Abuse	Questionnaire	Self-report measure developed by study authors
Luciano & Savage, 2007	Bullying	Questionnaire	The My Life in School checklist(S. Sharp, 1994)
Mannarino 1996	Sexual Abuse	Referrals from social services	N/A
Mcnally 2006	Sexual Abuse	Semi-structured interview	N/A
Marsh 2011	Bullying	Questionnaire	Adolescent peer relations (APRI) developed for study
Moran & Eckenrode, 1992	Multiple	Questionnaire	Not reported
Moyer	Sexual Abuse	Referrals from social services	N/A
Muller 1994	Physical Abuse	Questionnaire	Conflict Tactic Scale(Murray Straus & Christine Smith, 1990)
Porter & Long, 1999	Sexual Abuse	Questionnaire	Life experiences questionnaire (developed by study authors)
Radliff, Wang, & Swearer, 2016	Bullying	Questionnaire	The Verbal and Physical Bullying Scale–Victimization scale (Swearer et al., 2008)
Roazzi, 2016	Multiple	Referrals from social services	N/A
Rucklidge, 2006	Multiple	Questionnaire	Childhood Trauma Questionnaire(Bernstein et al., 1997)
Yamasaki et al	Bullying	Questionnaire	Olweus Bully/Victim Questionnaire(Solberg & Olweus, 2003)

Figure 4.4 Funnel Plot of Distribution of Effects of Childhood Trauma and Locus of Control Meta-Analysis



Appendix 5 Supplementary Information for Study III

Appendix Table 5.1 Correlation between belief-updating indices

Belief-updating indices[1]	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
Draws to Decision Task									
Average Draws to Decision (1)	-								
High cost of Sampling (2)	-0.50	-							
High decision Noise (3)	-0.28	-0.39	-						
Probability Estimation Task									
Contrary updating (4)	-0.28	0.13	0.18	-					
High expectation of reversal (5)	-0.12	0.08	0.27	0.60	-				
Adjustment Rate (6)	-0.27	0.18	0.08	0.64	0.24	-			
Inference Window (7)	0.04	-0.03	-0.05	-0.04	-0.03	-0.23	-		
Confidence (8)	0.02	-0.07	0.20	-0.04	-0.06	0.09	-0.42	-	
Decision Noise (9)	-0.23	0.06	0.1	0.25	-0.13	0.27	-0.07	0.18	-

Appendix Table 5.2 Belief-updating processes and frequent or distressing PEs at age 24 years (complete case n=1,652*)

	Unadjusted Model			Adjusted Model*		
	Odds Ratio	95% CI	P-value	Odds Ratio	95% CI	P-Value
Draws to Decision Task						
Cost of Sampling (top 10%)	0.74	0.39,1.41	0.363	0.70	0.37,1.34	0.282
Decision Noise (top 10%)	2.31	1.20,4.44	0.013	2.11	1.07,4.13	0.030
Probability Estimation Task						
Expectation of reversal (top 10%)	1.15	0.49,2.73	0.746	1.04	0.43,2.49	0.936
Adjustment Rate	0.24	0.02,2.85	0.257	0.22	0.02,2.65	0.233
Confidence (high or low)	1.01	0.65,1.56	0.981	1.02	0.66,1.57	0.933
Inference Length	1.06	0.79,1.43	0.681	1.04	0.77,1.40	0.782
Decision Noise	1.08	0.84,1.40	0.531	1.05	0.81,1.37	0.702

**Adjusted for Working Memory, IQ, executive functioning, sex, social class, crowded living conditions, income, genetic risk for SCZ, and maternal education

Appendix Table 5.3 Exposure to Trauma (0-17) and Belief-updating processes on Draws to Decision Task (complete case n= 1,652)

	Unadjusted Model			Adjusted Model*		
	Odds Ratio	95% CI	P-Value	Odds Ratio	95% CI	P-Value
Average Draws to Decision	-0.06	-0.12,0.01	0.083	-0.05	-0.12,0.01	0.125
Cost of Sampling (top 10%)	0.97	0.88,1.07	0.576	0.98	0.89,1.08	0.641
Decision Noise (top 10%)	1.17	1.03,1.34	0.018	1.15	1.00,1.32	0.044
Contrary Updating	0.01	-0.05,0.08	0.669	0.01	-0.06,0.07	0.811
Decision Noise	0.03	-0.01,0.08	0.149	0.03	-0.02,0.07	0.261
Expectations of Reversal (top 10%)**	1.01	0.87,1.16	0.938	1.00	0.86,1.16	0.960
Adjustment Rate	0.00	-0.00,0.01	0.204	0.00	-0.00,0.01	0.180
Confidence in Estimations (high)***	-0.04	-0.13,0.06	0.451	-0.03	-0.13,0.07	0.516
Confidence in Estimations (low)***	-0.08	-0.26,0.11	0.413	-0.08	-0.27,0.11	0.398
Inference Length (1-2)***	-0.04	-0.16,0.09	0.560	-0.05	-0.17,0.08	0.467
Inference Length (3-4)***	-0.04	-0.14,0.05	0.351	-0.06	-0.15,0.04	0.240

*Adjusted for Working Memory, executive function, IQ, sex, income, crowding, social class and maternal education

Appendix Table 5.4 Unadjusted results from Bivariate analysis of belief-updating indices and hallucinations and delusions

Belief-updating indices[1, 2]	Odds Ratio	95% CI	P-value	Odds Ratio	95% CI	P-value	P value (hall. vs delusions)
Draws to Decision Task	Hallucinations			Delusions			
Average draws to decision	0.91	0.82,1.00	0.061	1.00	0.89,1.12	0.967	0.777
High cost of Sampling	0.86	0.59, 1.25	0.419	0.88	0.58, 1.34	0.555	0.912
High decision Noise	1.69	1.10, 2.59	0.016	1.50	0.92, 2.45	0.108	0.672
Probability Estimation Task							
Contrary updating	1.05	0.96,1.15	0.273	1.04	0.94,1.15	0.437	0.869
High expectation of reversal	1.77	1.16, 2.71	0.009	2.04	1.29 ,3.21	0.002	0.605
Adjustment Rate	1.03	0.26, 4.16	0.965	0.47	0.09, 2.31	0.351	0.402
Inference Window (1-2)	0.98	0.60, 1.59	0.940	1.26	0.76, 2.10	0.372	0.794
Inference Window (2-4)	1.19	0.84. 1.69	0.333	1.14	0.76, 1.71	0.519	0.794
Low confidence	1.02	0.72, 1.44	0.280	1.23	0.84, 1.81	0.930	0.353
High confidence	0.67	0.31, 1.47	0.822	0.91	0.42, 2.01	0.883	0.353
Decision Noise	1.09	0.94, 1.27	0.248	1.09	0.92 ,1.29	0.297	0.993

Note: Imputed sample n=2,872 [1]Binary measures: Decision noise (DTD task), cost of sampling and expectation of reversal. Continuous measures: adjustment rate, decision noise (probability estimation task). Confidence and inference window measures are categorical measures, each with two outcomes of interest.